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SYSTEMATIZED AMYLOIDOSIS OF THE SKIN AND MUSCLES

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Systematized amyloidosis is the name which Lubarsch proposed for a form of amyloidosis which was atypical for generalized amyloidosis, but which involved far too much tissue to be classed as a localized form. The cases of systematized amyloidosis observed by Lubarsch [1] had certain features in common, thus establishing a fairly well defined syndrome; but specific cutaneous manifestations were not constant, although they were present in a high percentage of the patients observed.

Generalized amyloidosis, as originally described, consisted of changes in the large abdominal viscera accompanying such diseases as syphilis, tuberculosis, blastomas and some chronic suppurations. These diseases apparently have the faculty of altering protein metabolism in such a way as to produce amyloid.

Atypical deposits of amyloid were soon recognized, and Ziegler [2] called attention to the most common form when, in 1875, he demonstrated amyloid deposits strictly limited to the tongue and larynx. Such isolated involvement has since been observed in the heart, lungs, intestines and several other organs. Lindwurm,[3] as early as 1862, observed amyloid deposits in the skin; since then other authors have written on cutaneous amyloidosis, but only within the last few years has the subject attracted considerable attention. To be sure, cases are rare, in spite of the more diligent search for them. Dr. Winer [4] of our clinic recently

From the Division of Dermatology, University of Minnesota.

Read at the Fifty-Sixth Annual Meeting of the American Dermatological Association, Chicago, June 9, 1933.

1. Lubarsch, O.: Zur Kenntnis ungewöhnlicher Amyloidablagerungen, Virchows Arch. f. path. Anat. **271**:867, 1929.

2. Ziegler, E.: Amyloid Tumorbildung in der Zunge und dem Kehlkopf; Ein Beitrag zur Lehre von der amyloiden Degeneration, Virchows Arch. f. path. Anat. **65**:273, 1875.

3. Lindwurm: Hypertrophie und Ulceration der Haut mit amyloider Degeneration, Ztschr. f. rat. med. **14**:257, 1862.

4. Winer, L. H.: Local Amyloidosis of the Skin, Arch. Dermat. & Syph. **23**: 866 (May) 1931.

reported a case of localized cutaneous amyloidosis observed in Professor Oppenheim's department in Vienna. This paper, so far as we know, was the first one on the subject in the American literature.

CLASSIFICATION

For practical purposes, it seems permissible to divide cases showing amyloid changes in the skin into three large classes:

I. Localized amyloidosis cutis
  A. Primary or independent type
  B. Secondary type
II. Generalized amyloidosis with cutaneous involvement
III. Systematized amyloidosis with cutaneous lesions

I. *Localized Cutaneous Amyloidosis.*—This is a chronic benign condition, and because of the good general health of the patients it may be due to a difference in the nature of the amyloid itself, as Frieboes [5] suggested. Most of the strictly localized, or primary, forms of cutaneous amyloidosis described to date can be grouped under so-called lichen amyloidosis (Freudenthal [6]) or amyloidosis cutis nodularis et disseminata (Gutmann [7]). Clinically, these forms resemble lichen chronicus simplex, papular prurigo or even lichen planus; whether the amyloid deposit is the sole cause of the manifest lesions or whether it is secondary to a previous inflammatory process is not settled.

Koenigstein [8] believes that localized amyloidosis of the lichenoid variety is an independent dermatosis having slight variations but fairly well fixed characteristics and histologic features.

Freudenthal examined tissues from patients with a variety of cutaneous conditions for amyloid and found it present in certain keratoses and epitheliomas, especially cylindromas, and in some long-standing dermatoses. He observed amyloid almost exclusively in his searches in lesions occurring on exposed parts, but was unable to determine a cause. Although senile amyloidosis (Freudenthal) is a localized condition, there is a secondary deposit of amyloid in an already diseased skin.

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5. Frieboes, W.: Lehrbuch der Haut und Geschlechtskrankheiten, Leipzig, F. C. W. Vogel, 1930, p. 408.

6. Freudenthal, W.: Amyloid in der Haut, Arch. f. Dermat. u. Syph. **162**:40, 1930.

7. Gutmann, C.: Ein neuer Beitrag zur Frage der örtlichen Amyloidosis der Haut, Dermat. Wchnschr. **89**:1255, 1929.

8. Koenigstein, H.: (*a*) Ueber Amyloidablagerung als pathologische-anatomischer Befund bei Dermatosen, Wien. klin. Wchnschr. **34**:157, 1921; (*b*) Ueber Amyloidose der Haut, Arch. f. Dermat. u. Syph. **148**:330, 1924-1925; (*c*) Amyloid der Haut, in Jadassohn, J.: Handbuch der Haut und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 4, p. 254.

II. *Generalized Amyloidosis with Cutaneous Involvement.*—In the generalized amyloidosis which has been observed by internists and pathologists exanthems have been seen, but they have not been characteristic enough and their descriptions have not been sufficiently adequate to allow one to consider them diagnostic of the underlying cause. The papular eruption which is characteristic of localized amyloidosis has not been observed as yet in the generalized form.

Dr. Madden of our clinic observed a 19 year old girl at the Gillette State Hospital who had suffered from tuberculous disease of the left hip joint for fifteen years in whom generalized amyloidosis developed, with involvement of the thyroid gland, the liver, the spleen and the kidneys. For three weeks before death there had been a firm irregular swelling of the lower lip, just below the vermilion border, which later proved to be due to an amyloid deposit.

Fig. 1.—Nodular type of amyloidosis in a patient with generalized tuberculosis.

It will be noted that there is in this case an underlying cause for generalized amyloidosis with diffuse nodular lesions of the lip due to a marked local amyloid deposit. This case is an example of the type of cutaneous involvement which might be part of a generalized amyloidosis and may be contrasted with the changes observed in systematized amyloidosis.

III. *Systematized Amyloidosis.*—Lubarsch, in reviewing the atypical forms of amyloidosis, established certain criteria by which this type might be identified. He applied the term systematized amyloidosis to a syndrome which is based on a diffuse, widely disseminated, but not generalized, amyloid deposit. The term is somewhat misleading, because it denotes not a form of amyloidosis in which only a single system of organs is attacked, but a condition which presents the following features, which are constantly found in the reported cases: (*a*) little or no involvement of the organs which are usually diseased in generalized amyloidosis; (*b*) the presence of amyloid in organs which are ordinarily spared in the commoner form; (*c*) papular or nodular distribution of the amyloid deposits, with the frequent development of lesions in the skin, on the mucous membranes or at mucocutaneous junctures, due

to deep-seated amyloid deposits; (*d*) failure of these deposits to react in the ordinary manner to the accepted stains for amyloid, and (*e*) inability to demonstrate etiologic factors or concurrent diseases to account for the amyloid changes (Christian [9] has pointed out that in some cases of "generalized" amyloidosis no cause can be found).

Koenigstein gave the first clear description of a group of cases which represent this type of amyloidosis. Lubarsch,[1] Pick,[10] Gerstel,[11] Mollow and Lebell [12] and Gottron [13] have since contributed to the literature on the subject, so that now one may formulate a fairly well fixed set of symptoms and signs which are present with certain regularity and which give to this group the characteristics of an independent entity, even though the etiologic factor is wanting. The findings may be enumerated as follows:

1. A cutaneous eruption is present, which begins as a shiny, smooth, firm, flat-topped or spherical papule of waxy color, which, because of its tenseness, has the appearance of a translucent vesicle. These lesions consist of plaques which vary in size from that of a pea to that of a rather large sugar loaf. In some cases bands of the same general character have been noted. They resembled the sheath type of scleroderma. The regions about the eye, nose and mouth, as well as the mucocutaneous junctures, were the areas commonly involved.

2. Glossitis with macroglossia is an almost constant, as well as an early, symptom. The tongue becomes painful and is greatly enlarged. There are areas of subepithelial hemorrhage. Deep furrows and fissures form, and a necrotic-looking purulent deposit may form on certain spots but not over the entire tongue. The mucosal side of the lips and cheeks has a similar hypertrophic appearance.

3. Pains and aches in the back produced by marked amyloid changes in the heavy skeletal muscles are a common and bitter complaint of these patients. The cardiac musculature may be damaged, causing cardiac insufficiency, and involvement of the smooth muscles of the intestinal tract may cause severe constipation, accompanied in some cases by marked hemorrhage.

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9. Christian, H. A.: The Nephrosis Syndrome Associated with Idiopathic Amyloidosis, M. Clin. North America **15**:805, 1932.

10. Pick, L.: Ueber atypische Amyloidablagerung, Klin. Wchnschr. **10**:1515, 1931.

11. Gerstel, G.: Ueber atypische Lokalisation des Amyloids, insbesondere über die Makroglossia amyloides diffusa, Virchows Arch. f. path. Anat. **283**:466, 1932.

12. Mollow, W., and Lebell: Zur Kinik der systematisierten Amyloidablagerung, Wien. Arch. f. inn. Med. **22**:205, 1932.

13. Gottron, H.: Systematisierte Haut-Muskel-Amyloidose unter dem Bilde eines Sklerodermа amyloidosum, Arch. f. Dermat. u. Syph. **166**:584, 1932.

4. Purpuric lesions due to ecchymoses or subepithelial hemorrhages are common. They are located at points which are subject to minor, but more or less constant, bruising, such as the extremities, the tongue and the buccal mucosa.

5. A progressive and downward course, with intensification of all the symptoms and the production of severe secondary symptoms, has been observed in all the reported cases.

LITERATURE

In order to show the constancy of the symptoms of systematized amyloidosis just enumerated, we shall briefly review the cases reported to date.

Koenigstein [8b] carefully reviewed the literature on cutaneous amyloidosis and added two cases which he pointed out should be sharply separated from the localized form of the condition. In 1924 he described a patient whose striking initial symptom was pain in the shoulders, arms and hands. The patient was aware of the fact that he was losing strength and that talking, chewing and swallowing were becoming distressing because of gradual but progressive enlargement of the tongue and the development of elevated plaques on the oral mucosa. Subsequently he lost much weight, became weak and was extremely constipated, although later he had periods of diarrhea. There was marked albuminuria. The patient finally died with ileus and complicating pneumonia. Postmortem examination revealed amyloidosis of the gastrointestinal tract, the heart and the striped muscles of the trunk. Even the urinary and vascular systems were involved. The liver, spleen and kidneys were free from amyloid—a striking fact. There was an extensive eruption of transparent, opalescent, sharply defined papules about the eyes and mouth and on the neck, the fingers, the extensor side of the extremities and the trunk. The tongue was greatly enlarged and was notched and fissured, and there were many small elevated plaques on the buccal mucosa.

In Koenigstein's second case the symptoms were similar, with the addition of marked bleeding from the mouth and purpuric subcutaneous extravasations of blood on the trunk. This patient also became weak. The tongue and oral mucosa were much thickened and fissured. The cutaneous lesions consisted of shiny distinct papules which later coalesced into rather large diffuse plaques. Atrophy resulted, and hemorrhages into the skin were present. Absorption brought about scarring of a polycyclic type. Albuminuria, generalized edema and other signs of cardiac insufficiency developed. The case terminated fatally.

Lubarsch,[1] in 1929, described two similar cases. One patient had macroglossia, thickened oral mucosa and purpuric hemorrhages in the

skin and mucous membranes. The second patient had no clinical cutaneous signs except purpuric spots on the hands and body and in the mouth. Microscopic deposits of amyloid were later observed in the skin, tongue, heart and gastro-intestinal tract.

Pick,[10] in 1931, discussed the pathologic changes encountered in a case which was later described by Gerstel.[11] The initial symptom was sudden marked enlargement of the tongue, followed by a diffuse firm thickening of the skin of the neck. Symptoms of ileus developed, and the patient was sent to the hospital for further study. Subsequently purpura developed, but no albuminuria was present. At autopsy amyloid was observed throughout the heart, lungs and gastro-intestinal tract, as well as in the skin and tongue.

Mollow and Lebell,[12] in 1932, observed a patient who had a papular eruption, macroglossia with dysphagia, constipation accompanied by abdominal pain, albuminuria and tense stiffness of the muscles. On microscopic examination a marked amyloid deposit was observed throughout the entire gastro-intestinal tract, and other organs having considerable muscular tissue were involved to a lesser degree. Small amounts of amyloid were observed in the smaller blood vessels of the entire body and in the bone marrow.

Gottron,[13] in 1932, also described such a case. His patient was a woman whose history, while not irrelevant, gave no hint as to the causal factor. She had had menstrual difficulties for many years, also intestinal and rectal pain, and had suffered from transient pains in the back for several years when standing or walking. Symptoms of nephritis with cardiac insufficiency appeared about the same time that thickening of the face and neck was observed. The patient became worse, and the tongue began to enlarge. The cutaneous lesions were papules as well as plaques, and appeared as purpuric spots on the fingers. Albuminuria was present. Roentgenologic studies of the digestive tract suggested intramural changes. The patient was still living at the time the report was made.

PATHOLOGY

The chemical structure of amyloid is not at yet fully established. It is a protein substance, rich in tyrosine and diamino-acids, and its chemical nature varies somewhat in different anatomic locations. Perhaps there are different phases in its cycle of production, which give changing microchemical and staining properties. The substance stands in close relationship to the large group of hyalins which are transparent and homogeneous, and can be identified only by staining. It is colored grayish yellow with the van Gieson stain, from red to purple with methyl or gentian violet, from brownish yellow to mahogany with iodine, from blue to violet with iodine and sulphuric acid and deep pink with congo red.

Macroscopically organs infiltrated by amyloid appear on section to be made up of glassy masses of different arrangement and amounts. The volume of the organ is increased. Microscopically, amyloid appears in the shape of cylinders, flakes or rods and takes on the general form of collagen or muscle fibers, or, if the tissue substance is lost, it fills the space. Besides the usual amorphous deposits, a crystalline type has been described by Maximow [14] in horse liver.

Amyloidosis is a disease of the blood vessel-connective tissue apparatus. Most frequently the small arterioles are involved at their capillary ends. The larger vessels, too, may be diseased. The arteries are involved more often than the veins. The supporting structures and the musculature are not directly diseased, but the amyloid is deposited in, or seeps into, the lymph spaces and by its growth or increase brings about atrophy or even complete destruction.

REPORT OF A CASE

The following case is that of a patient [15] who had signs and symptoms which we believe would justify the diagnosis of systematized amyloidosis with involvement of the skin and muscles:

A Jewish man, 54 years of age, born in Russia, had enjoyed good health until December, 1930, when he became aware of a dull pain in both hips and across the lumbar region. The same dull, aching pain was later felt in the knees and shoulders, and the hands became tender and stiff. The past history was of no significance. In 1931, his tongue became painful, especially on eating, and began to enlarge gradually. His fingers became tensely swollen and tender, and small, localized purpuric spots appeared following the slightest trauma. He suffered from stubborn constipation, and the urine showed albumin. He entered the medical wards of the Minneapolis General Hospital, where a diagnosis of chronic arthritis and glomerulonephritis was made.

In October he appeared at the Minnesota General Hospital and was sent to the Dermatology Clinic because of an eruption on the hands and about the eyes. He was admitted to the medical wards, which were then under Dr. Hilding Berglund, who mentioned localized amyloidosis as a possible explanation for the enlarged tongue. At this time the striking symptoms were marked weakness, pain in the lumbar region and joints, macroglossia, constipation, proteinuria and an eruption about the eyelids, which consisted of firm, yellow, waxy, translucent, spherical papules; these were increasing in size. The patient was in and out of the hospital from October, 1931, until July, 1932. Each successive observation revealed marked accentuation of the previous symptoms. The weakness progressed to prostration. The greatly enlarged tongue made swallowing and speech almost impossible. The eruption involved the face and scalp and the anal and genital regions. The hands were much swollen; the joints could be flexed only a little, and there were numerous small purpuric lesions. Constipation was marked, although there had been a short period of diarrhea. At no time could the liver and spleen be palpated, nor

14. Maximow, quoted by Koenigstein.[8a]

15. This patient (M. G.) was twice presented at meetings of the Minnesota Dermatological Society (Arch. Dermat. & Syph. **25**:1133 [June] and **26**:1133 [Dec.] 1932).

was it possible to demonstrate enlargement on roentgen examination of the abdomen. The protein in the urine was of the Bence-Jones type, and Dr. Grace Medes of the department of medicine reported as follows:

"During the entire time the patient was under observation he had a marked proteinuria. The protein, tested by the method described by Osgood and Haskins (1922), reacted as a typical Bence-Jones protein; that is, it precipitated at room temperature upon the addition of acetic acid and sodium chloride to the urine, it dissolved upon subsequent heating to the boiling point, and redissolved upon cooling. In view of the absence of conclusive symptoms of multiple myeloma in the patient and the general resemblance of his condition to amyloidosis, this test was repeated numerous times, and on all occasions pure Bence-Jones protein was found. Upon being salted out fractionally with ascending concentrations of sodium sulphate, the protein also behaved as the Bence-Jones type, as shown in the table. According to this, 24.4 per cent salts out at a concentration of Na_2SO_4 at which pseudoglobulin I of the plasma is precipitated (1.25 molar) and 75.1 per cent at a concentration at which pseudoglobulin II of the plasma precipitates (1.55 molar). This salting-out curve does not differentiate this protein from amyloid, since the latter also salts out in this area.[16]

Results of Testing Protein with Ascending Concentrations of Sodium Sulphate

Test	Sodium Sulphate, Molar Concentration	Protein Remaining in Solution, per Cent
1	0.75	100.0
2	1.00	99.6
3	1.25	75.2
4	1.55	0

"Samples of the protein were salted out from urine by saturating the latter with Na_2SO_4, decanting the supernatant liquid and washing the protein in frequent changes of saturated Na_2SO_4. The protein was then dialyzed against distilled water at 10 C., and the purified protein dried rapidly before fans in a current of warmed air. The dried protein gives the typical test for Bence-Jones protein, as described in paragraph 1. It gives the following staining reactions: no color with compound solution of iodine, no color with congo red and bright purple with methyl violet. Other samples of purified Bence-Jones protein from patients with multiple myeloma reacted similarly.

"The plasma proteins of this patient were normal with respect to their salting out, except for a slightly elevated fibrinogen. The total protein was 7.63 Gm. per 100 cc. of plasma; the fibrinogen was 0.78; the euglobulin, 0.38; the pseudoglobulin I, 0.89; the pseudoglobulin II, 1.55 and the albumin, 4.03. Serum calcium determinations were: on Nov. 3, 1931, 12.7 mg. per 100 cc. of serum; on November 17, 12.7 mg., and on November 19, 13.2 mg.

"Glomerular filtration, as shown by Rehberg's method, was 115 cc. per minute on Nov. 4, 1931, 73 cc. on Jan. 28, 1932, and 38 cc. on July 19, 1932. These changes are typical of those shown by patients with multiple myeloma, regardless of whether they are excreting Bence-Jones protein. At no time did this patient show a retention of metabolites, the nonprotein nitrogen of the blood varying around 25 mg. per 100 cc.

16. Bannick, E. G., and Barker, N. W.: Diffuse Amyloidosis of Unknown Etiology, M. Clin. North America **14**:773, 1930.

"The patient under consideration showed chemical findings similar to those in multiple myeloma. There were normal or slightly elevated serum calcium, lowered glomerular filtration and Bence-Jones protein in the urine. The latter behaved in all respects similarly to that of patients with multiple myeloma."

The intravenous congo red test according to the method of Bennhold was carried out on several occasions. On the first admission to the hospital only 13 per cent of the dye was removed from the blood stream after one hour (from 10 to 40 per cent may be removed in normal persons).[17] On repetition of the test eight months later, more than 90 per cent of the dye was removed; this might be considered a specific test for the presence of large amounts of amyloid substance in the body. When it was repeated within seven days, only 20 per cent of the dye was removed, which may be explained on the basis of saturation of the amyloid deposits by the dye introduced previously, since it is known that it may be retained

Fig. 2.—Condition of tongue of author's patient at onset of disease. Note lesions about the eyelids.

for three months or longer.[18] The test was performed for the fourth time six weeks later, and 47 per cent of the dye was taken out of the blood stream. This was regarded as definite confirmation of the results of the second test.

When the patient was first seen, the cutaneous lesions consisted of a row of spherical papules situated along the border of the lower eyelids. The papules were firm and tense and had a waxlike shiny appearance. The overlying skin was stretched and thin, giving the lesion a translucent vesicular appearance. As the condition of the patient became worse, the cutaneous lesions became larger. They assumed a cubical shape and were whiter and softer. At no time was there any ulceration, exudation or blister formation.

17. Vivoli, D.: Congo Red as Diagnostic Measure in Amyloidosis, Rev. sud.-am. de méd. et de chir **3**:208, 1932.

18. Hardgrove, M. A. F.: Retention of Congo Red in Amyloid Disease, Arch. Path. **15**:238 (Feb.) 1933.

Fig. 3.—Nodular lesions on the buccal mucosa.

Fig. 4.—Hemorrhagic type of lesion on the fingers.

Purpuric lesions were to be found on the fingers and toes. They were noted as small stellate collections of blood just below the epithelium. The overlying skin became dry and crustlike, and when it came away no scar was to be seen. No ulcers or keratoses resulted.

The buccal and anal mucosal lesions were practically the same as the advanced cutaneous lesions and could be characterized as sharply outlined, elevated, yellow, soft cuboidal plaques. Here and there localized hemorrhagic spots were to be found in the nodes. Deep clefts developed between some of the adjacent nodes.

At first the tongue was slightly enlarged and covered with small translucent papules and localized purpuric spots. As the process advanced the tongue became much larger; deep furrows developed which corresponded to the clefts between the buccal nodes, and small areas became denuded and covered with a pyogenic membrane as the result of injury. This, of course, was secondary. At the end the tongue was about twice its normal size.

Repeated examinations of the blood gave normal results as to cytology, bleeding and clotting time. Because of the Bence-Jones proteinuria, roentgen examination of nearly the entire bony skeleton was carried out; this showed, in addition to

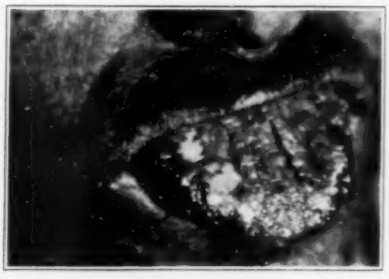

Fig. 5.—Progressive enlargement of the tongue a year after onset.

a slight degree of hypertrophic arthritis, diffuse osteoporosis of the lumbar spine, pelvis and femur. Dr. Leo Rigler later reported: "Some rarefaction is present around the hip joints, in the pelvis and in the pubic bones. Some similar process is present at the distal end of the humerus. The ribs also show some decalcification of a very peculiar character. The whole appearance suggests most strongly bone atrophy from disuse. The possibility, however, of a very diffuse universal infiltration of the bones from some such process as myeloma cannot be entirely excluded, as it might occur without any more definite findings than are shown here."

The patient was miserable and dejected. No drugs gave him comfort. He could not roll over in bed. He refused to stay in the hospital and died at home. No postmortem examination was allowed, but the family physician reported death as being due to ileus and intestinal hemorrhage.

HISTOLOGY

For microscopic study, biospsy sections were taken from the tongue, the buccal mucosa and the anal mucocutaneous juncture, and a purpuric lesion of the hand was also excised. Fixation was in 70 per cent alcohol. In addition to the usual stains, special studies were made, all of the tried stains for amyloid being used. Sections were taken to Vienna to Professor Geiger, who verified the presence of amyloid in all the tissues mentioned.

It must be emphasized that in order to ascertain the presence of amyloid, a technic of staining must be mastered. We used the methods advocated in Schmorl's book.[19] The greatest difficulty is found in staining a section and having the amyloid retain its selective coloring matter. We found that staining with diluted solutions of gentian violet and congo red gives the best sections for study, but discovered that it is advisable to examine the preparation instantly after staining, even without a cover slip.

The Skin.—There was a moderate degree of hyperkeratosis, especially in the lesions removed from the hands. The striking factor was the homogeneization of the entire cutis. With the congo red stain, it was noticed that almost the entire cutis was made up of amyloid. This was deposited in the manner of normal collagen. The blood vessels were dilated, and in the walls of the larger vessels there was a decided amount of amyloid. Here and there areas of free red blood corpuscles were noted. A few polymorphonuclear and round cells were scattered throughout the cutis. In the sections from Dr. Winer's patient with localized amyloidosis, amyloid was present only in the upper papillary portion of the cutis, and then only in localized areas, while in our patient amyloid was uniformly deposited throughout the cutis—in fact, there was no portion of the cutis that was free in the sections examined. With the elastic tissue stain, the fibers were seen to be somewhat diminished, but were still present.

The Tongue.—In sections from the tongue the entire subepithelial area was taken up by amyloid; this apparently had been laid down in irregular masses, which had coalesced. Deep in the musculature, amyloid was observed between the bundles of muscles, lying in much the same manner as in the cutis. The amyloid was noted to be especially heavy about the vessels. The staining with congo red was not uniform; some areas were deep scarlet, while here and there were pale pink islands. There was more cellular infiltrate in the sections from the tongue, which probably may be accounted for by the marked fissuring and trauma. From our examination of these sections, we would consider that the spaces between the connective tissue and the musculature had been filled with amyloid, bringing about a certain amount of atrophy, but the amyloid could not be considered in the sense of an amyloid tumor.

Summary.—In summarizing the histologic change of the skin and mucous membrane in our case, we would state that the most striking and important change was the marked amyloid deposit in the subepithelial tissues. All other changes may be looked on as secondary and were not of great significance.

COMMENT

On reviewing the observations in this case and in other cases, we must emphasize the age of the patients—from 46 to 66 years. It is noted that all were middle-aged or older. Sex and race seem to be of no significance, nor is geographic location. The initial symptom which appears often in the reports is marked and progressive weakness; this went on to prostration in our patient. It is probably associated with amyloidosis of the skeletal muscles. Purpuric lesions, especially at points of frequent minor trauma, are common. This is probably due to injury

19. Schmorl, G.: Die pathologisch-histologischen Untersuchungsmethoden, Leipzig, F. C. W. Vogel, 1928.

of the small walls of arterioles by the amyloid deposit. In our patient purpuric spots were constantly present on the hands and the tongue, and perhaps the severe intestinal hemorrhage may be accounted for in the same way. The marked constipation and fecal incontinence toward the end may be explained by the fact that the intestinal musculature was involved in this type of amyloidosis, as in almost every patient examined post mortem.

Careful and exhaustive clinical and laboratory studies did not shed any light on the cause of this syndrome. Tuberculosis and syphilis were excluded, as was malaria.

The significance of Bence-Jones proteinuria in our case is not entirely clear; Bence-Jones protein is rarely found in diseases other than multiple myelomas. This condition has been of little interest to dermatologists, although Bloch,[20] in 1909, described a papular eruption on the trunk and extremities of a patient with Bence-Jones proteinuria. This eruption did not resemble amyloidosis cutis in its usual form and has not been recognized as such in the literature. It involuted spontaneously, leaving localized atrophic areas somewhat similar to those seen in one of Koenigstein's cases. Microscopic examination showed marked degeneration of the elastic tissue, which Bloch regarded as a toxic change resulting from the Bence-Jones protein. He was unable to demonstrate any evidence of multiple myeloma, although the patient complained of diffuse pains along the bones. The patient died after two years and the postmortem observations were later reviewed by Glaus [21] (1917), who noted definite myelomatous changes in the bones, as well as amyloid deposits in the tongue, gastro-intestinal tract, bone marrow, heart, lungs and skeletal musculature. In the large abdominal organs amyloid was observed only in the walls of the small vessels. The elastic changes previously described by Bloch were observed in the skin and in some organs.

The relationship of Bence-Jones protein to amyloid is not established. Hyalin, amyloid and this protein are closely allied. Hyalin has often been seen in the tumor masses of multiple myelomas and elsewhere in the tissues of these patients.[22]

Magnus-Levy [23] reviewed the reported cases of multiple myelomas showing amyloid deposits and discussed the relationship of Bence-Jones

20. Bloch, B.: Ueber eine bisher nicht beschriebene, mit eigentümlichen Elastinveränderungen einhergehende Dermatose bei Bench Jonesscher Albuminurie, Arch. f. Dermat. u. Syph. **99**:9, 1909.

21. Glaus, A.: Ueber multiple Myelozytom mit eigenartigen, zum Teil kristallähnlichen Zelleinlagerungen, Virchows Arch. f. path. Anat. **223**:301, 1917.

22. Leupold, E.: Amyloid und Hyalin, Ergebn. d. allg. Path. u. path. Anat. **21**:120, 1925.

23. Magnus-Levy, A.: Bence Jones Eiweiss und Amyloid, Ztschr. f. klin. Med. **116**:510, 1931.

proteinuria and these deposits, holding that the number of cases favored a definite relationship and not merely an association. He suggested that Bence-Jones protein deposited in bone may be transformed into amyloid. The distribution of these amyloid deposits was of interest to us because of the similarity to the distribution in systematized amyloidosis, even though cutaneous lesions had not been described. It must be remembered that systematized amyloidosis, such as that described by Lubarsch, included such cases as those of Kenn, Landau, Beneke, Lubarsch (case 3), Wild [24] and Steinhaus,[25] and similar cases have since been reported by Warren [26] and Pick (case 1). In all these cases there was no cutaneous involvement, although amyloid was present in the skeletal, cardiac and vascular musculature or in the smooth muscles of the gastro-intestinal, respiratory and genito-urinary system. There is thus a striking similarity between the distribution of the amyloid deposits in patients having multiple myelomas and in systematized amyloidosis, but a definite relationship has not been clearly established, although it is strongly suggested.

In comparing the Bloch and Glaus case with ours, we found no resemblance in the cutaneous findings, but could conceive of the condition which they described as being the form of amyloidosis cutis observed in Koenigstein's second case, in which atrophic changes followed involution of a papular eruption. As in our case, Bloch was unable to demonstrate multiple myelomas ante mortem, although in both cases careful Roentgen studies were made because of the finding of Bence-Jones proteinuria. The amyloid deposits observed at autopsy in the earlier case were similar to those usually present in systematized amyloidosis and were probably similar to those in our case. The important difference was Glaus' opportunity to examine bone marrow at autopsy and demonstrate myelomatous changes. He regarded the amyloid deposits as the results of toxic changes brought about by the myelomas, and that was the conception of most investigators who observed amyloid in patients with myelomas. This theory is reasonable, in that other blastomas (and leukemia, carcinoma and Hodgkin's disease) occasionally produce amyloidosis. The difference lies in the fact that the latter processes are associated with the usual form of generalized amyloidosis, while the myelomas are associated with amyloid deposits of the nature of those observed in systematized amyloidosis, the resemblance being most striking in Bloch's case.

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24. Wild, C.: Beitrag zur Kenntnis der amyloiden und der hyalinen Degeneration des Bindegewebes, Beitr. z. path. Anat. u. z. allg. Path. **1**:177, 1886.

25. Steinhaus, F.: Ueber eine seltene Form von Amyloid- und Hyalin- Infiltration am Circulations- und Digestionsapparat, Ztschr. f. klin. Med. **45**:375, 1902.

26. Warren, S.: Generalized Amyloidosis of the Muscular Systems, Am. J. Path. **6**:161, 1930.

If one remembers the close chemical relationship between Bence-Jones protein and amyloid and accepts the belief of Magnus-Levy and others that these represent different stages in the formation of the same end-product, the way is open for many hypotheses. It is possible that further and more accurate studies on the relationship of myelomas, Bence-Jones proteinuria and systematized amyloidosis may lead to a demonstration of the essential differences between generalized and systematized amyloidosis or toward an understanding of the basic principles of the entire problem of amyloidosis.

ABSTRACT OF DISCUSSION

Dr. John H. Stokes, Philadelphia: Has Dr. Michelson had occasion to study syphilitic macroglossia associated with general amyloid change? What was the serologic status of his patient? I ask because in a recently observed case of macroglossia in a man, aged 68, which was thought to be associated with Hodgkin's disease of the submaxillary and sublingual lymph nodes, but in which the patient was found to have a strongly positive Wassermann reaction, we later recognized the brawny wooden induration of the muscles of the lumbar region, buttocks and thighs which is associated with generalized amyloidosis accompanied by macroglossia Under bismuth (not arsphenamine) therapy the patient's neck, which required a size sixteen collar, has shrunk to its original dimensions (size fifteen); the sublingual induration has been reduced 30 per cent, and the buttocks and thighs have softened and become more pliable. The process has not completely involuted, of course, since the amyloid change, if present, is probably irremediable. We have not yet been able to perform a biopsy.

Dr. Samuel E. Sweitzer, Minneapolis: Amyloid is a somewhat mysterious substance of which little is known. I do not think that we know how it is formed, and we have been unable to produce it by animal experimentation. This patient was shown twice before the Minnesota Dermatological Society, and we were unable to make an immediate diagnosis. He also visited the Mayo Clinic, and the physicians there were also unable to make a diagnosis. We tried to discover why we could not make a diagnosis in this case immediately. Staining for amyloid was done early, but apparently we were not staining properly. About two years ago, Dr. Winer, one of my colleagues, wrote an article on amyloidosis of the skin; at that time we thought that we knew how to stain for amyloid, but in this case we were unsuccessful. There is great variation on staining, and it is difficult to determine the strength of the staining solution. We are more interested in the common cases of amyloidosis of the skin than in the case which Dr. Michelson has reported. Only a few cases similar to his have been reported, as the condition is rare. In the common cases the eruption looks like lichen chronicus simplex. There is severe itching, and the condition does not respond to roentgen therapy. The common cases are the ones in which help is likely to be sought. We have examined a number of these cases, but were able to find only one that showed amyloid.

Dr. Sigmund Pollitzer, New York: The subject of staining amyloid recalls to my mind the fact that in the early days of pathologic anatomy I took a course in Virchow's laboratory. All the material was from the morgue; this was poor material, according to present ideas, but all Virchow's great work was based on the study of dead material. One of the methods which we used in staining the

liver, in which amyloid degeneration occurs rather commonly, was to take a bottle of iodine and pour the fluid over the cut surface of the liver; it immediately brought out the amyloid deposit. This must be done with fresh material only and without embedding the material. I suppose that if pieces of fresh tissue from Dr. Michelson's patient had been placed on a slide and if iodine had been poured over them, it would have shown the amyloid deposit immediately.

Dr. Henry E. Michelson, Minneapolis: The condition that Dr. Stokes describes evidently was not due to amyloid, because he said that the patient was greatly improved. Amyloidosis is a progressive process, and reports of regression due to true resorption of the amyloid are much doubted. Amyloidosis due to syphilis is, of course, the generalized type and does not disappear with antisyphilitic treatment. Dr. Pollitzer is correct in stating that Virchow was a pioneer worker on amyloid. We discussed the difficulty in staining that Dr. Sweitzer mentioned.

MYELOID LEUKEMIA WITH CUTANEOUS MANIFESTATIONS

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Three types of cutaneous manifestations have been described as being associated with myelogenous leukemia. Of these, two are the result of infiltration of the cutis, subcutis and appendages of the skin by myelogenous cells: (1) the circumscribed, nodular variety, which is the more frequent one, and (2) diffuse, infiltrative erythrodermia, resembling seborrheic dermatitis, of which but one example has been reported. These types are identified as specific or true myelosis of the skin. The third type is the nonspecific or toxic eruption, which may present itself in the form of vesicles, papules, or pustules or as a small or large subdermal hemorrhage, and which shows no characteristic histologic structure.

The case presented here belongs to the first variety—the circumscribed, nodular group of true myelosis.

In presenting it we want to emphasize the necessity of correlation of the clinical features and the laboratory findings, both of which are essential in establishing this diagnosis. A review of the literature is on the same basis. This brings to light an important prognostic sign, previously noted by Weil and Isch-Wall,[1] i. e., that the appearance of specific myelosis of the skin heralds an acute phase or exacerbation of myelogenous leukemia and that the life expectancy of the patient is only a few months.

REPORT OF CASE

History.—Mrs. A. P., an Austrian, 50 years of age, had been in poor physical condition for three years. She had lost 25 pounds (11.3 Kg.). Moderate exertion caused fatigue, and edema of the ankles was noted in the evening. She had a dragging sensation in the left side of the abdomen and was troubled with gas.

From the Pittsburgh Skin and Cancer Foundation.

1. Weil, P. É., and Isch-Wall, P.: Un cas de leucémie myélogène chronique avec poussée terminale de tumeurs cutanées et leucémie aiguë, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:84 (Jan. 26) 1931.

These symptoms had progressed in severity. Nocturia from three to five times a night had been present for two years. In July 1931 an infection developed in the deep layers of the skin of the palm of the left hand which drained for six months and resulted in a partial atrophy of the left hand and forearm. On June 10, 1932, the patient noticed a mass in the left axilla. The mass became bothersome, but was not painful. An itching eruption appeared in the axilla and extended over the adjoining portion of the chest and inner aspect of the arm. On Aug. 12, 1932, she presented herself at the Pittsburgh Skin and Cancer Foundation for treatment.

The family history was negative for blood dyscrasia. The patient's father died of cancer of the stomach. The patient was married and had three children, all living and well. Menses did not appear from January to August, 1932, but in August there was a period which lasted for seven days.

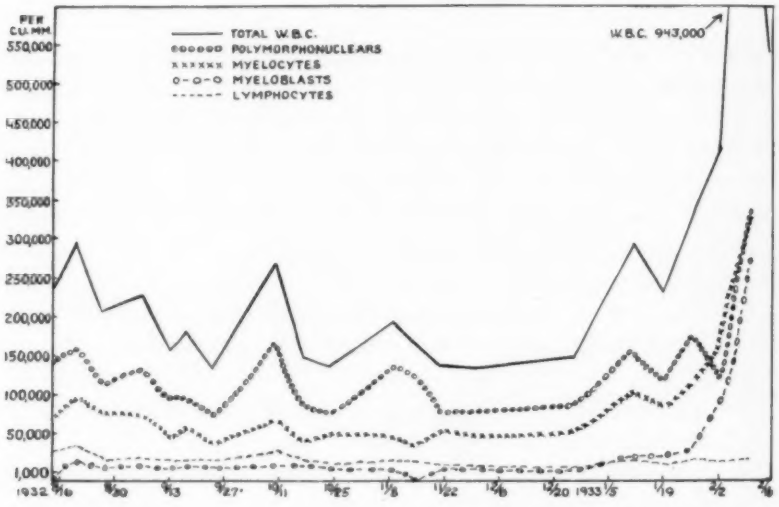

Fig. 1.—The trend of the total white blood cell counts and the actual number of the various types of white blood cells.

Physical Examination.—The patient was a pale, emaciated woman weighing 100 pounds (45.4 Kg.). A moderate arcus senilis was present. The oral hygiene was fair. The chest was thin, and the lungs were clear. The heart was normal. The blood pressure was 110 systolic and 80 diastolic, and the pulse rate 100. The spleen was greatly enlarged, extending almost to the midline and downward to the level of the umbilicus. The surface was smooth, and no notch could be felt. The liver was palpable three fingerbreadths below the costal margin. No free fluid was noted in the abdominal cavity. The anterior cervical lymph glands were slightly enlarged, and the inguinal glands were palpable. In the left axilla a mass the size of an egg was palpable. The mass was nodular, as though composed of numerous lymph glands, and was well fixed to the deep structures. No cutaneous lesions were present at this time. The left forearm and hand were noticeably atrophic, and a small, well healed scar was present in the palm of the left hand.

Laboratory Examination.—The urine showed an acid reaction, and had a specific gravity of 1.011. A trace of albumin and occasional white blood cells were evident

on microscopic examination. Examination of the blood revealed: white cells, 235,000; red cells, 3,810,000; hemoglobin, 50 per cent (Sahli), and color index, 0.65. The differential cell count was: polymorphonuclear neutrophils, 48 per cent; neutrophilic myelocytes, 13 per cent; eosinophilic myelocytes, 5.2 per cent; basophilic myelocytes, 4.6 per cent; metamyelocytes, 4.8 per cent; lymphocytes, 4.2 per cent; monocytes, 3.8 per cent; eosinophils, 6.8 per cent, and basophils, 10 per cent. The red cells varied greatly in size and shape, with a marked tendency to microcytosis, achromia and polychromasia. Thirty-one normoblasts were seen while counting 1,000 white cells. The reaction to the Kahn test was negative. Analysis of the gastric secretion demonstrated: free hydrochloric acid, 16 degrees; combined acid, 24 degrees, and total acid, 40 degrees.

Roentgenograms of the chest showed a fine, beadlike infiltration of the upper lobes, indicating old, healed tuberculosis of the lungs. A domelike distortion of

Fig. 2.—Distribution of the lesions.

the right side of the diaphragm suggested pulmonary adhesions or a defect due to enlargement of the liver.

Clinical Impression.—A diagnosis was made of chronic myelogenous leukemia, old bilateral pulmonary tuberculosis, old pleural adhesions on the right side with distortion of the diaphragm and an old abscess of the left palm with atrophy of the left forearm and hand.

Treatment and Clinical Progress.—Superficial roentgen therapy (84 kilovolts, 4 milliamperes and a 5 mm. aluminum filter at a distance of 14 inches [35.56 cm.] for twelve minutes) was begun over the long bones. Treatment by the same dosage was repeated at intervals of from three to seven days from Aug. 16, 1932, to Feb. 10, 1933. Twenty-six treatments were given. Alternate areas were chosen for roentgen exposure: the lower right side of the pelvis and spleen, left supraclavicular region and lower portion of the left femur; the right supraclavicular region, lower portion of the right femur and left axilla, etc.

On August 24 an abscess of the upper left bicuspid tooth was incised and drained. On September 12 it appeared advisable to extract the abscessed tooth. The patient's general condition had declined. The bleeding and the coagulation time were normal. Following dental extraction there was some bleeding, which was not easily controlled. Calcium gluconate, 6 cc., was given intravenously daily for three days. Cod liver oil and viosterol, in addition to a high caloric diet, were given in an attempt to increase the nutritional state of the patient.

On October 5 arthritic pains in the left shoulder and swelling of the left wrist appeared, and during the following two weeks gradually subsided.

During the period of observation and treatment there was a general decrease in the white blood cell count to a level of 175,000 cells per cubic millimeter. The

Fig. 3.—Close view of the lesions on the chest.

differential counts maintained a fairly constant proportion of white blood cells, with a large number of late myelocytes and polymorphonuclear leukocytes. Figure 1 illustrates the trend of the total white cell counts and gives a graphic representation of the actual number of the various types of white blood cells. From November 11 to December 30 the total level fell to 150,000, and a stable differential count was maintained, indicating a constant maturing factor in the granular blood cells.

On November 2 the patient was examined carefully, and ten bluish, slightly elevated, firm nodules were observed over the left breast. They were painless and nonpruriginous. These lesions progressively increased in size and in number, so that within three months the greater portion of the wall of the chest, the left and right axillae and the inner surface of the forearm were involved. Some of the

lesions coalesced, forming a somewhat larger nodule over which the skin was movable in areas; some lost their bluish color and became waxy; some even disappeared entirely, leaving no stain or scar, but most of them persisted.

On Jan. 9, 1933, one of the nodules in the skin was excised for biopsy. Examination showed a massive infiltration of the derma and subderma with myeloblasts and myelocytes. Sections of the nodules in the skin showed only a slight thinning of the epidermis. The rete pegs were still fairly well preserved between the papillae of the corium.

The infiltrating cells which occasioned the formation of the nodules consisted of immature examples of the myeloid series. The predominating form was the nongranular myeloblast, a mononuclear cell with a rounded to ovoid vesicular nucleus and a moderately abundant bland cytoplasm. There were scattered eosinophilic mononuclear myelocytes mingled with the less mature myeloblastic forms,

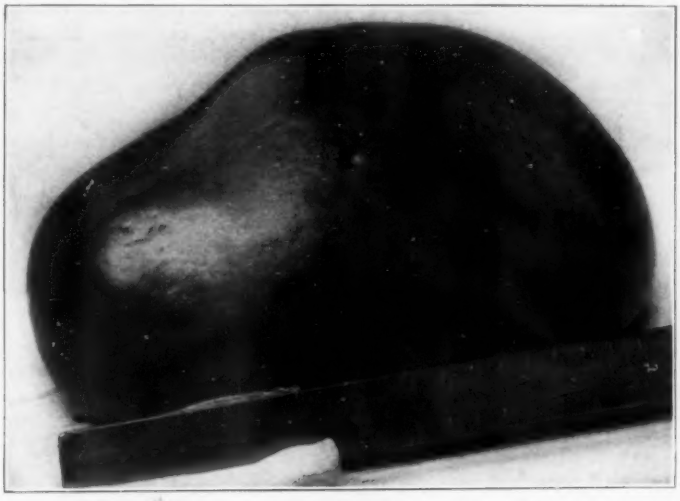

Fig. 4.—Photograph showing the size of the spleen.

but these were not numerous. There were also some eosinophils and polymorphonuclear neutrophils among the infiltrating cells. In characteristic and well developed nodules the infiltration by myeloid cells of the types enumerated was dense and massive; and it extended from just beneath the epidermis throughout the corium.

There was a well marked tendency of the cell masses to be larger and more closely packed in the lymphatic spaces and in the tissues about the vessels, hair follicles and coil glands and in the nerve fibers. This was more distinctly seen at the margins of the nodules, where the general infiltration was less diffuse. Myeloid cells also infiltrated some of the more superficial lobules of the subcutaneous adipose tissue.

The corium was, of course, much widened in the areas of nodular infiltration, but no proliferation of the connective tissue or other change was evident.

At this time the total white blood cell count began a steady increase despite treatment. The early stage of this increase was due to the increase in the polymorphonuclear leukocytes and myelocytes. On January 25 the rate of total

increase in cells became extreme, and a rapid increase in the total number of myeloblasts indicated a lack of maturation of the granulocytes. The myeloblasts were large, pale staining cells with a single nucleus and clear cytoplasm in Wright's stain. Peroxidase stain revealed varying numbers of peroxidase granules. This reaction indicated a reversion to the type of reaction of the white cells seen in acute leukemia. Associated with it the patient became very ill. A temperature of 100 F. and edema of the ankles developed, and the patient became sufficiently short of breath on exertion to be confined to bed.

On February 2 a second nodule was removed, and at the same time a section of the uninvolved surface of the skin of the right thigh was obtained for biopsy. The latter was normal histologically, while the former again showed the presence of myeloblastic and myelocytic cell infiltration.

On February 10 the patient was admitted to Mercy Hospital. The temperature ranged from 100 to 102 F., the pulse rate from 100 to 128 a minute and the respiratory rate from 24 to 40. She was extremely emaciated and orthopneic,

Fig. 5.—The bone marrow, as revealed at autopsy.

and was moribund with complete heart failure. The size of the spleen, liver and peripheral lymph glands had not changed perceptibly during recent months. The patient was drowsy and toxic. The red blood cell count had decreased and produced the typical anemia of the disease, with 3,020,000 cells per cubic millimeter and 28 per cent hemoglobin (Dare). The patient died on February 16, eleven months after the onset of the illness and thirteen weeks after the appearance of the nodules on the skin.

Diagnosis.—The diagnosis was chronic myelogenous leukemia, leukemia cutis, secondary anemia and circulatory failure.

Autopsy (Dr. H. H. Permar).—The enlarged liver and greatly enlarged spleen appeared to fill the abdominal cavity. The spleen weighed 1,850 Gm. and measured 23 by 16 by 9 cm. The outer surface was smooth and the organ felt firm. On section the mottled dark red surface was marked by depressed, lighter areas the size of a pinhead. On microscopic examination the typical picture of myelogenous leukemia was seen, with a loss of normal structure and infiltration of the pulp with all types of myelogenous cells. With peroxidase stain large single nucleated cells were revealed as myeloblasts. Numerous nucleated red cells were present, and the blood vessels were filled with granulocytes. A number of small infarcts were present.

The liver weighed 3,100 Gm. and measured 27 by 26 by 8 cm. The organ was firm. The cut surface bulged and was marked by red, depressed areas the size of a pinhead. Microscopic sections showed the sinusoids to be filled with all types of myelogenous cells, the picture being identical with that in the sinuses of the spleen.

The lymph nodes of the mesenteric, perigastric, peribronchial, and retroperitoneal regions were enlarged and firm. They varied from 1 to 2 cm. in size, and each gland remained discrete. The outer surfaces were whitish and smooth. The cut surfaces were whitish and moist. Microscopic section revealed the normal gland structure replaced by a massive infiltration of the pulp by myeloid cells of all types, as seen in the spleen.

The bone marrow of the femur was pinkish on gross examination. The normal fatty structure was replaced by an almost solid overgrowth of myeloid cells. Red blood cell centers were seen as small areas containing nucleated cells. No areas of necrosis were present.

Sections of the nodules on the skin were remarkable because of a heavy infiltration of myeloblasts, myelocytes and polymorphonuclear leukocytes into the subcutaneous layer. The cells formed into nodules in the subcutis and extended into the cutis. Cells of the same type were scattered in the tissue spaces, lymphatics and blood vessels.

The pancreas, kidneys and suprarenal glands showed a general infiltration of tissue by myelogenous cells of all types and a filling of the blood vessels by the same type of cells.

The lungs showed some congestion and an increase in the fibrous tissue of the alveolar walls. No exudate was present in the structure. Myeloid cells filled the blood vessels. Other organs revealed nothing of importance aside from the usual changes corresponding to the age of the patient.

Summary.—This case represents a true picture of chronic myelogenous leukemia with marked splenomegaly and enlargement of the liver. Other typical changes were hyperplasia of the bone marrow, lymphadenopathy, and myeloid cell infiltration of the organs. An interesting and rare associated reaction was the specific cutaneous picture.

COMMENTS ON LEUKEMIA

The development of the present concept of leukemia has been marked by definite steps from the first observation of the disease in 1845. Virchow and Bennett, working independently, described cases at autopsy in which there was enlargement of the spleen, with increased numbers of white blood cells and a peculiar white appearance of the blood. Virchow, in 1853, described a type in which the lymph glands were principally involved and the spleen to a lesser degree, and designated two types of leukemia—lymphatic and splenic. Neumann, in 1870, noted changes in the bone marrow in the splenic type and proposed the term myelogenous leukemia. The classification during this period was based primarily on clinical differences.

The second step was the distinction by Ehrlich, in 1891, of two principal types of leukemia by examination of the blood: myelogenous leukemia with hyperplasia of the white cells in the bone marrow (granulocytes), and lymphatic leukemia with an increase of lymphatic cells. Recognition of certain atypical cells of the blood was difficult, and much confusion existed in the classification of many cases. The term "mixed leukemia" was used to cover the cases in which early cells could not be designated definitely as being of myelogenous or lymphatic origin. Pappenheim and others believed that both cell types developed from a single undifferentiated parent cell, giving rise to morphologic confusion.

Naegeli, in 1912, was the first to point out that the myeloblast, the earliest recognizable cell of the myelogenous (granular) series of cells, was a nongranular cell and was often confused with the lymphoblast, although it had a different origin. This observation more adequately clarified the previous confusion. The final step in development came in 1916, when Graham was successful in preparing a simple clinical method for the peroxidase stain. With this stain the cells of the myelogenous series contain peroxidase granules while the cells of the lymphatic series contain no peroxidase granules. One source of error is still present, however. It is known that the earliest myeloblasts may not have developed the peroxidase ferment, and thus will give a negative reaction to a peroxidase stain. Such instances are not common, and when they occur, a careful study of the morphologic features of these cells in comparison with typical cells of known myelogenous origin in the same patient will lead to their proper classification.

Until fairly recent times accuracy in hematologic classification has been difficult. Progress has been marked by simplification and by an increased knowledge of finer morphologic distinctions. In recent years there have been more adherents to the dualistic theory of cell development. It seems important to outline briefly the criteria for morphologic classification of the blood cells when stained by Wright's stain.

The myelogenous series of cells, originating in the bone marrow, passes through successive stages from the parent cell, the myeloblast, to the myelocyte, metamyelocyte and polymorphonuclear leukocyte. The myeloblast is a large, pale staining cell, with a relatively large single nucleus and clear cytoplasm. The myelocyte stage is similar in size and nuclear structure, but the cytoplasm produces one of three types of granules: neutrophilic, eosinophilic or basophilic. These three types of cells pass through a single nuclear metamyelocytic stage to the final stage as immature and then mature segmented polymorphonuclear leukocytes with their distinctive granularity.

The lymphatic series of cells, originating in the bone marrow and lymphatic organs, passes from the parent cell, the lymphoblast, directly into the large and small lymphocyte. The lymphoblast is a large, pale-staining cell, in all morphologic respects like a myeloblast. The lymphocyte has a single round, well stained, sharply outlined nucleus and a varying amount of clear blue cytoplasm. Frequently a few large red granules are present in the cytoplasm.

Leukemia is now considered a disease of the blood-forming organs, in which there is proliferation of the white blood cells with a decrease in the maturation of the cells. Normally only mature cells are passed into the peripheral circulation. In leukemia immature and premature cells appear in varying numbers in the peripheral circulation, associated with the typical clinical features of the disease.

The clinical manifestations of acute myelogenous and acute lymphatic leukemia are similar. The condition occurs principally in young persons, the onset being marked by fever, malaise and rapid prostration. Inflammation and ulceration of the oral mucous membrane with hemorrhage into the mucosa and gross bleeding from the mouth are most common. The lymph glands and spleen may be palpable. The total blood cell count is usually above 50,000 cells. Examination of the blood smear offers the means of classification. The presence of the embryonal cell types with a predominance of myeloblasts or lymphoblasts is most characteristic, while more mature cells of the corresponding cell series are present in a smaller percentage. More positive identification is usually made, however, with the peroxidase stain. Not uncommonly the blood cells may be of such immature development as to make classification uncertain. If such is the case after careful morphologic study, a positive differentiation can be made only at biopsy or at autopsy.

In an occasional case showing the typical clinical and hematologic features of one type of leukemia a normal or low white cell count may exist. This condition has been called aleukemic leukemia. It is now generally believed to be a stage of leukemia in which cells do not enter the peripheral circulation, although the bone marrow and tissues at this time show the changes characteristic of leukemia. An increase in the cell count usually develops after a varying period, and the typical blood picture appears. Should a patient die in the aleukemic phase of the disease, a positive diagnosis can be made only on examination of the tissue at autopsy.

In chronic leukemia the clinical features of the two types are usually distinguishable. In myelogenous leukemia the enlargement of the spleen is characteristic, while the lymph nodes are normal or only slightly enlarged. In lymphatic leukemia local or general enlargement of the lymph node is most characteristic, with only a moderate enlargement of the spleen. However, cases are seen in which these distinctions are

not clearly manifest. There may be enlargement of the lymph nodes of the myelogenous form, or the enlargement of the lymph glands may be localized in the mediastinum and retroperitoneal regions in the lymphatic form. Classification by means of study of the blood becomes extremely important. In chronic leukemia there is a greater proportion of mature and late immature cells in the circulating blood. Myelocytes and metamyelocytes are more numerous in the myelogenous form, while lymphocytes are more numerous in the lymphatic form. There may be periods in which more embryonal cells appear in greater numbers, and frequently the acute type of blood response is seen as a terminal feature, as demonstrated in our case.

The importance of correlating the clinical fetaures of the disease with the hematologic observations must be emphasized. In a disease involving the production of white cells such a correlation must be made to exclude certain cases of infection or sepsis in which the blood-forming centers may temporarily admit premature cells into the circulation; the so-called "leukemoid" or "leukemia-like" reactions are examples.

Anemia of the secondary type develops as an associated condition in leukemia and may be severe. An outstanding feature is the presence of a great number of nucleated red blood cells. Variation in the size, shape and staining of the blood cells is marked.

CASES IN THE LITERATURE

A careful search of the literature for unquestionable cases of myelosis cutis revealed the following reports:

CASE 1 (Bruusgaard [2]).—A man, 38 years old, had been ill for several months. The leukocyte count was 410,000, of which 60 per cent were myelocytic mononuclear neutrophils. The spleen and the submaxillary and inguinal lymph nodes were enlarged. On the trunk and arms numerous bluish, isolated and confluent nodules were present. Biopsy showed that the subcutaneous tissue, hair follicles, sweat glands and skin contained extensive accumulations of mononuclear neutrophilic myelocytes, which gave a positive oxidase reaction. Autopsy confirmed the diagnosis.

CASE 2 (Burckhardt [3]).—A man, 37 years old, had been ill for two and a half months. Study of the blood revealed: neutrophilic myelocytes, 74.6 per cent; eosinophilic myelocytes, 2.2 per cent, and myeloblasts, 4 per cent. The spleen, the liver and the lymphatic nodes were enlarged. A generalized eruption was present which resembled a seborrheic dermatitis with marked infiltration. Myelocytes and polymorphonuclear neutrophils were found in the perivascular infiltration. The patient lived for two and a half months. Autopsy confirmed the diagnosis.

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2. Bruusgaard, E.: Ueber Hauteruptionen bei der myeloiden Leukämie und der malignen Granulomatose, Arch. f. Dermat. u. Syph. **106**:105, 1911.

3. Burckhardt, J. L.: Zur Frage der akuten myeloiden Leukämie, Frankfurt. Ztschr. f. Path. **6**:167, 1911.

CASE 3 (Gotthold and Herxheimer [4]).—In a man, 60 years old, the leukocyte count was from 7,300 to 71,000, of which from 60 to 70 per cent were polymorphonuclear neutrophils and from 2 to 3 per cent eosinophils. The liver and spleen were enlarged. On the nape of the neck and on the body many nodules from the size of a pinhead to that of a baby's fist were present. Microscopic examination of the nodules showed the myeloid type of cells. Autopsy confirmed the diagnosis of myeloblastic leukemia.

CASE 4 (Lubliner [5]).—A girl, 17 years old, had been ill for seven months. The leukocyte count varied from 44,000 to 116,000, of which 17 per cent were polymorphonuclears, from 13 to 74 per cent myeloblasts and 35 per cent myelocytes. The liver, spleen and lymphatic glands were enlarged. Numerous bluish-red or brown nodules of fibrocartilaginous consistency were present, distributed irregularly. Histologic examination of the nodules showed a perivascular infiltration. The cells were chiefly myelocytes and myeloblasts. One lymphatic gland showed almost complete transformation of tissue.

CASE 5 (Saphier and Seyderhelm [6]).—A woman, 47 years old, had been ill for one year. The leukocyte count was 280,000, 58 per cent of which were myeloid cells. The spleen was enlarged. On the dorsum of the nose, on the cheeks and later on the forehead there were reddish, hard and painless nodules ranging in size from that of a lentil to that of a pea. The patient lived for eleven days after the skin became involved. Histologic examination of the nodules showed the corium to be thinned out. In the deeper layers and in the subcutaneous tissue was a cellular infiltration which consisted chiefly of cells of the myeloid series. Autopsy confirmed the diagnosis.

CASE 6 (Bruusgaard [7]).—In a man, 30 years old, the leukocyte count was 70,000, of which 85.6 per cent were myelocytes, 6.2 per cent myeloblasts and 1 per cent eosinophils. Practically all the lymphatic glands were enlarged. Many hard, bluish, elastic, purpuric, infiltrated lesions were present on the thighs and dorsum of the body. The skin and subcutaneous tissue showed profuse perivascular infiltration with myeloblasts, myelocytes, neutrophils and eosinophils.

CASE 7 (Ketron and Gay [8]).—A woman, 63 years old, had been ill for two years. The leukocyte count was from 3,180 to 68,740, from 50 per cent to 92.5 per cent of which were myeloid cells. The liver and the spleen were enlarged, and there was slight lymphatic adenopathy. A great number of bluish-gray nodules and hemorrhagic spots ranging in size from that of a pinhead to that of a pea appeared, first on the upper part of the abdomen and lower thoracic region and later over the entire body. The patient lived for four months after the skin became involved. Histologic examination showed an infiltration of the cutis and subcuta-

4. Herxheimer, G.: Ueber die Lymphoblasten (grosszellig-lymphatische) und Myeloblastenleukämie, München. med. Wchnschr. **60**:2506 and 2573, 1913.

5. Lubliner: Ein Fall von atypischer chronischer myeloischer Leukämie mit zahlreichen Hauteruptionen und Uebergang in Myeloblastenleukämie, Folia haemat. 1. Teil (Archiv) **22**:15, 1917-1918.

6. Saphier, J., and Seyderhelm, R.: München. med. Wchnschr. **67**:69 (Jan. 16) 1920.

7. Bruusgaard, E.: Demonstration eines Falles von myeloider Leukämie mit Purpura und myeloiden Hautinfiltraten, Acta dermat.-venereol. **2**:273, 1921.

8. Ketron, Lloyd W., and Gay, Leslie N.: Myeloid Leukemia of the Skin, Arch. Dermat. & Syph. **7**:176 (Feb.) 1923.

neous tissue by myelocytes, lymphocytes, large phagocytic cells and curiously degenerated eosinophils. The myelocytes gave a positive oxidase reaction. Autopsy confirmed the diagnosis.

CASE 8 (Almkvist and Arzt[9]).—A man, 39 years old, had been ill for about four and a half years. The leukocyte count was 53,000, of which 6 per cent were myeloblasts, 14 per cent myelocytes and 56 per cent primitive myelocytes. The liver, spleen and lymphatic glands were enlarged. Livid blue and skin-colored nodules, ranging in size from that of a pea to that of a bean, and of hard consistency were sparsely distributed over the breasts, abdomen and upper parts of the thighs. He lived for three months after the skin became involved. Histologic examination showed a pronounced infiltration by lymphocytes between the cutis and subcutis. In the deeper areas of the skin a markedly polymorphic infiltration was found; the majority of the cells showed granular cytoplasm. Giemsa stain showed granules to be present in the early myeloid cells. Autopsy confirmed the diagnosis.

CASE 9 (Hartmann[10]).—In a man, 31 years old, the leukocyte count was 162,000, of which 82 per cent were neutrophils, 15 per cent myelocytes and 2 per cent eosinophils. Several crops of yellowish nodules varying in size from that of a lentil to that of a cherry were present on the upper lip, cheek, forearms and legs. Improvement was followed by a relapse and involvement of the thorax and forearms. Biopsy specimens showed an infiltration of cells around the hair follicles and other appendages of the skin. The capillaries were markedly dilated. Autopsy confirmed the diagnosis.

CASE 10 (Arzt[11]).—A man, 50 years old, had been ill for three years. The leukocyte count was 269,000, of which 8 per cent were myeloblasts and 22 per cent myelocytes. The spleen, liver and lymph glands were enlarged. A large number of pale or brownish-red lesions, ranging in size from that of a cherry to that of a nut, were present all over the body. The patient lived for two months after the skin became involved. Biopsy specimens showed the derma to be thickly infiltrated with myelocytes, myeloblasts and large cells. Autopsy confirmed the diagnosis.

CASE 11 (Sannicandro[12]).—A man, 25 years old, had been ill for two years. The leukocyte count was 560,000, of which 3 per cent were neutrophils and 52 per cent myelocytes. The spleen and liver were enlarged, but the lymphatic glands were not. Many yellowish vesicles, papules, papulopustules and nodules varying in size from that of a pea to that of a nut were distributed over the body. Histologic examination of the lesions showed a polymorphic process. Myeloblastic infiltration was present.

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9. Almkvist, J., and Arzt, L.: Skin Manifestations in Leukemic Affections, Brit. J. Dermat. **36**:428, 1924.

10. Hartmann, E.: Ueber die Einteilung der myeloischleukämischen Erkrankungen der Haut vom dermatologischklinischen Gesichtspunkt, Dermat. Ztschr. **49**:52 (Oct.) 1926.

11. Arzt, L.: Myelosarcomatose oder leukämische Myelose, Arch. f. Dermat. u. Syph. **155**:233, 1928.

12. Sannicandro, G.: Cutaneous Manifestations, Gior. ital. di dermat. e sifil. **69**:1397 (Oct.) 1928.

CASE 12 (Arzt [13]).—A woman, 20 years old, had been ill for three and a half months. The leukocyte count was 5,200, of which 90 per cent were myeloid cells. The spleen was not enlarged, but the liver and lymph glands were. A fair number of bluish-gray macules and papules from the size of a pea to that of a bean were present over the body, but were most marked over the breasts. The patient lived for one month after the skin became involved. A biopsy specimen revealed an infiltration of the subderma. The cells resembled a normal lymphocyte; they gave a positive oxidase reaction. Autopsy confirmed the diagnosis.

CASE 13 (Nekam [14]).—A woman, 62 years old, had been ill for fifteen days. The leukocytes were 21,000 and later 2,200, of which 94 per cent were myeloblasts. The spleen and liver were enlarged. Numerous bluish, brownish and pale yellow nodules from the size of a pea to that of a bean were present over the breasts and thighs, and later over the arms and lower extremities. The patient lived for fifteen days after the skin became involved. A biopsy specimen revealed a heavy infiltration of nongranular, early myeloblastic cells in the lower strata of the corium and in the sweat and sebaceous glands. The oxidase reaction was negative. Autopsy confirmed the diagnosis.

CASE 14 (Barney [15]).—A man, 55 years old, had been ill for six months. The leukocyte count was from 24,600 to 83,000, of which from 10 to 31 per cent were neutrophilic leukocytes, from 1 to 3 per cent eosinophilic myelocytes and from 1 to 7 per cent myeloblasts. The liver was enlarged. The lymph glands were slightly enlarged. A fair number of brown to purple, noninflammatory, painless nodules ranging in size from that of a pinhead to that of a cherry were present over the trunk, thighs, upper part of the arms and buccal mucosa. The patient lived for two months after the skin became involved. A biopsy specimen revealed the corium to be infiltrated with myelogenous cells which gave a positive reaction to oxidase.

COMMENT

The appearance of a nodular eruption in our patient ushered in the terminal acute exacerbation of myelogenous leukemia, and the decline became progressive and rapid. When this course is compared with that in other cases reported in the literature the length of life after the appearance of specific cutaneous manifestations appears relatively short. Therefore the internist should be aware of this prognostic sign.

In order to avoid confusion, and to establish beyond question the diagnosis of myelosis of the skin, the oxidase reaction should be determined, for except in the most immature cells of the myeloid series a positive reaction can be obtained.

Finally, we would reemphasize the symptom of dryness in the mouth which is annoying to the patient and which was progressive in our case.

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13. Arzt, L.: Specific Exanthems Developing in the Course of Leukemia Myelosis, Arch. f. Dermat. u. Syph. **160**:84, 1930.

14. Nekam, L. Jr.: Case with Involvement of the Skin, Dermat. Ztschr. **62**: 158 (Oct.) 1931.

15. Barney, Robert E.: Leukemic Myelosis Associated with Specific Nodules in the Skin, Arch. Dermat. & Syph. **27**:725 (May) 1933.

SUMMARY

A case of myelogenous leukemia, with the hemogram and results of biopsy and autopsy, was reported.

The subject of leukemia as related to the cellular elements was discussed.

The literature was reviewed from the standpoint of proved cases of true myelosis of the skin.

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PRACTICAL CLINICAL AND LABORATORY ASPECTS OF PRECIPITATION TESTS FOR SYPHILIS

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During the past ten years, precipitation tests for syphilis have been rapidly assuming a place of increasing importance in serodiagnosis. During this same period, the complement-fixation tests have also been undergoing modification and standardization. In clinical work the questions arise as to which tests to use and as to the relative reliance which may be placed on them. From the practical standpoint, any test must be judged by the following criteria: (1) sensitivity and specificity, (2) ease in reading results, (3) simplicity of performance (including the use of apparatus and biologic materials), (4) rapidity of performance and (5) the purpose for which the test is to be used. Obviously, a test which meets these requirements, is sufficiently sensitive and is easily performed will best meet the demands of the clinician. The amount of serum required for the test is sometimes also important, as in the case of infants.

Since the controversy raging at present on the exclusive use of precipitation tests or complement-fixation tests rests apparently on an immunologic basis, it is worth while to review briefly the theoretical basis on which the tests rest.

The existence of infection in the body stimulates the production of certain substances which possess the power to destroy or otherwise affect injuriously the disease-producing agent or to neutralize its poisons. They appear in the blood plasma and lymph. They may appear soon after the development of infection or they may be delayed until the disease is well advanced, and they may remain for a variable time after recovery.

These antibodies, or immune bodies, are specific in that each is produced only as a result of the activity within the body of a particular disease-producing agent or antigen, and they act against this antigen alone. Therefore, the presence of any of these immune bodies in a

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person's blood may, with certain exceptions, be regarded as pathognomonic of the corresponding disease.

These antibodies are usually described in terms of Ehrlich's theory. The agglutinins or precipitins belong to the second order and the complement-fixing or sensitizing antibodies to the third order.

The serum globulin of the syphilitic patient is apparently specifically altered, so that when placed in solution with lipoid particles it forms a denatured coating or film on them. The film apparently has the properties of antibodies of the second and the third order, as it is able to cause precipitation or clumping of the complex particles, and also to sensitize properly prepared antigens to the action of complement. Whether this syphilitic reagin is one substance with properties both of sensitizing for lysis and of precipitating, or whether it contains antibodies of both second and third orders, is still controversial.

ANTIGENS (HAPTENS)

Briefly defined, an antigen is any substance that causes the formation and appearance of antibodies in body fluids. Most antigens are highly specific, are colloids and are usually protein in nature. However, it was found experimentally that properly prepared, nonspecific, lipoidal dispersions could be used in vitro as antigens, though they are incapable of producing antibodies in vivo. The specificity of the serologic reactions is related to the specifically altered reagin in syphilitic serum and not to the hapten or antigen employed in the tests.

The lipoid, probably a lecithin, is obtained from dried, pooled beef heart powder which is first extracted with ether. An alcoholic extract is then obtained. This is the basis of the antigen used.

It was later found that the addition of small quantities of cholesterol markedly increased the sensitivity of the lipoidal antigen. Eagle [1] apparently worked out the nature of this sensitization thoroughly. He believed that the particles of cholesterol, in precipitating out in watery solution, form a nucleus about which a film of the lipoidal antigen develops. The effect of this is to increase the size of the lipoidal antigenic particles. This requires less syphilitic reagin and less agglutination to become visible.

MECHANISM OF PRECIPITATION

When normal serum is added to antigen, the serum proteins form a film about the lipoidal particles but remain water-soluble, are easily

1. Eagle, Harry: (*a*) Studies in the Serology of Syphilis: I. Mechanism of Flocculation Reactions, J. Exper. Med. **52**:717 (Nov.) 1930; (*b*) II. Physical Basis of Wassermann Reaction, ibid. **52**:739 (Nov.) 1930; (*c*) III. Fortifying Effect of Cholesterin on Antigen, ibid. **52**:747 (Nov.) 1930; (*d*) VI. Induction of Antibodies to Tissue Lipoids (Positive Wassermann Reaction) in Normal Rabbits, ibid. **55**:667 (April) 1932.

washed away and do not cause precipitation or agglutination. However, when syphilitic serum is added, the syphilitic reagin, which seems to be an altered fraction of the globulin, coats the lipoidal particles with an insoluble denatured protein film which, in the presence of electrolyte (salt solution), tends to agglutinate or precipitate into visible clumps. It is this clumping which forms the visible end-point of precipitation tests.

If complement and indicator are added to the precipitation test, the complement is fixed and the hemolysis is inhibited. Kolmer [2] expressed the belief that the fundamental mechanism of complement fixation in syphilis is identical with the colloidal flocculation reactions. Eagle was of the opinion that both complement fixation and precipitation are identical in nature, being merely different stages in the same chemical process. Levine [3] recently discussed an interesting theory as to the immunologic basis and value of complement fixation and precipitation.

VARIOUS TESTS

The practical application of precipitation to clinical serology has taken the form of a number of different methods and modifications which may be roughly divided into macroscopic or tube tests and microscopic tests. Of these, the microscopic tests have come more and more to the front in the past few years.

In the macroscopic group a number of tests have gained wide acceptance. Of these, the Kahn and Hinton tests have gained widest usage in America and the Sachs-Georgi and Meinicke tests in Europe. They are all closely related.

Kahn Test.[4]—Pooled, powdered beef heart is extracted first with ether and then with alcohol. The alcohol-soluble portion is retained and cholesterolized. The antigen is titrated with salt solution to determine the dilution of antigen which is optimal. The dilution is used which shows the smallest amount of salt solution in proportion to antigen having a precipitate which goes back into solution in salt solution, an unstable precipitation solution being most desirable. Serum from the patient is inactivated for thirty minutes at 56 C.; 0.85 per cent salt solution is used. Three tubes are set up containing equal amounts of serum but having dilutions of antigen of 3:1, 6:1 and 12:1, respectively. The tubes are shaken thoroughly for two minutes and incubated for fifteen minutes at 37 C. Readings are made on the amount of precipitate visible to the naked eye, a negative reaction showing a uniform opalescent solution. Antigen and serum controls are also set up.

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2. Kolmer, J. A.: Infection, Immunity and Biologic Therapy, Philadelphia, W. B. Saunders Company, 1924.

3. Levine, B. S.: Should Precipitation Tests for Syphilis Be Adopted to Exclusion of Complement Fixation Procedures? J. Clin. Path. **2**:319 (July) 1932.

4. Kahn, R. L.: Serum Diagnosis by Precipitation, Baltimore, Williams & Wilkins Company, 1928.

Hinton Test.[5]—The antigen for this test is an ether-insoluble, alcohol-soluble extract of beef muscle. The extract is cholesterolized and then glycerolated with a 50 per cent solution of glycerol. The preparation of this antigen takes from four to eight weeks. After this test is set up, a sixteen hour incubation period is required, and the reading must be made one hour after the incubation period. Exact maintenance of the incubation period is essential. A negative test shows uniform turbidity throughout the fluid or even a clearing of the fluid, but no sizable clumps. Clumping and flocculation visible to the eye denote a positive reaction.

Ball Reactions.—The Müller ball reaction is the most prominent of these tests. Kline[6] also described a test of similar nature which may be performed with his antigen. The Müller reaction requires a special antigen which is furnished only by the author of the test through a supply house in New York. These tests require special chilling and preparation of antigen-emulsions and careful mixing with centrifugation for an hour at a narrow range of speed. There are a number of technical difficulties which detract from the practicability of the test. A positive reaction shows a single ball of flocculated material floating in a clear solution. It is striking in strongly positive serums.

The Vernes test requires special apparatus in its performance and the Sachs-Georgi test seems to be somewhat less practicable than the Kahn test.

Among the microscopic tests, the Kline test[6] seems to be the most widely used. The antigen is rather difficult to prepare, and the process is tedious. It is an ether-insoluble, alcohol-soluble extract of pooled beef heart powder which is treated with acetone to obtain an acetone-insoluble wax, partially soluble in alcohol. The antigen contains 8 per cent of this wax. It is diluted and cholesterolized to make a working emulsion which retains its usefulness for from sixteen to forty-eight hours. A very sensitive emulsion may also be made up by further centrifugation and incubation. The serum and working emulsions together with a saline dilution are set up on paraffin rings on a glass slide, and, after a short period of agitation, are read with a low power microscope. A negative test shows a field of evenly distributed particles. The positive reaction shows large clumps of these particles in a relatively clear field.

Rosenthal Test.—A simple modification of the microscopic tests was recently introduced by Rosenthal[7] and studied by Tulipan and Director.[8] The antigen is an ether-insoluble, alcohol-soluble extract of pooled, powdered beef heart muscle which is kept as stock solution A. A 2 per cent solution of cholesterol in acetone is kept as stock solution B. The working emulsion is composed of equal parts of stock

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5. Hinton, W. A., and Stuart, G. O.: The Hinton Glycerol-Cholesterol Agglutination Reaction, J. Lab. & Clin. Med. **14**:621 (April) 1929. Hinton, W. A., and Berk, A.: Hinton Glycerol-Cholesterol Reaction for Syphilis; Second Modification, New England J. Med. **202**:1054 (May 29) 1930. Hinton, W. A. Hinton Test for Syphilis: Third Modification, J. Lab. & Clin. Med. **18**:198 (Nov.) 1932.

6. Kline, B. S.: Microscopic Slide Precipitation Tests for Syphilis, ed. 1, Baltimore, Williams & Wilkins Company, 1932.

7. Rosenthal, L.: Rapid Precipitation Test for Syphilis, Proc. Soc. Exper. Biol. & Med. **27**:61 (Oct.) 1929.

8. Tulipan, L., and Director, W.: Microprecipitation Test (Rosenthal) in Syphilis, Arch. Dermat. & Syph. **25**:451 (March) 1932.

solutions A and B; it is stable and may be used for two or three months. Paraffin rings on glass slides or hollow ground slides may be used. Five-hundredths cubic centimeter of serum is placed in the ring, and 1 small drop of working emulsion is added. The mixture is stirred, and the whole slide is agitated or rotated a few times. The test is read immediately and follows the criteria of the Kline readings.

EXPERIMENTAL WORK

It has been our custom to perform the Kolmer and the Kahn tests on serums of all patients seen in the clinic, with the modification that only the first two tubes and the control tube of the Kolmer test are used. The following experimental work was conducted to determine whether the Hinton, Kline, or Rosenthal tests had sufficient advantage over the Kahn test to warrant substitution of one of them as our precipitation test.

Two of us (E.B.R. and R.H.) conducted a study of the Kline, Hinton, Wassermann (Kolmer) and Kahn tests in 1,000 cases. The Kline test agreed with the clinical observations on the patients in 96.8 per cent of the cases. There was disagreement in 32 cases, in 9 of which the reactions might be considered falsely positive and in 18 of which there were negative reactions in proved cases of syphilis. The Kolmer test agreed with the clinical observations in 95.3 per cent of the cases. There was disagreement in 47 cases, in 5 of which there were false positive reactions and in 32 of which there were negative reactions in proved cases of syphilis. The Kahn test agreed with the clinical observations in 95.7 per cent of the cases. There was disagreement in 43 instances, in 2 of which there were false positive reactions. In a critical consideration of the group of 130 cases of syphilis, all 3 tests agreed in 62.3 per cent of the tests. The Hinton tests on 1,320 serums agreed with the clinical observations in 96.9 per cent of the cases. There were 5 false positive reactions.

The Kline test gave a higher percentage of positive reactions in syphilitic cases than the Kolmer or Kahn tests, but agreed closely with the reactions obtained with the Hinton test. However, the number of false positive reactions ranged slightly higher. The tendency toward false positive reactions and negative reactions in some cases of late syphilis should rule against the exclusive use of the precipitation test and should necessitate, at least for the present, a check test with complement fixation on every serum.

A series of about 800 Rosenthal tests were performed by one of us (J.M.v.d.E.) on serums simultaneously with the routine Kolmer and Kahn tests of the regular serologic laboratory of the clinic. In the first several hundred tests, a noticeable tendency to false positive readings was present. As acquaintance with the test increased and a definite technic was established, these became much less numerous. The last

604 tests were selected as being representative of the test. Three readings were made on each reaction, and if the reaction was positive, a check test was performed. Later, the reactions to the Kolmer and Kahn tests were ascertained and compared with the readings obtained with the Rosenthal test.

In this series, the results of the Rosenthal test agreed closely with those of the Kahn test. One frankly false positive reaction occurred. In 3 other cases the reading with the Rosenthal test was 1 plus, or doubtfully positive. One of these cases was that of a man of 40 who had been an excessive drinker and had precordial pain, a systolic blow to the left of the sternum and a blood pressure of 142 systolic and 70 diastolic. Determination of the basal metabolic rate showed it to be — 5 per cent. The 2 other cases, 1 of neurodermatitis and 1 of rectal fistula, gave irrelevant clinical histories as far as syphilis was concerned.

In 3 cases the Kahn test was definitely positive (an average of 2 plus), while the Rosenthal test was negative. In 15 cases the Kahn test was weakly or doubtfully positive, while the Rosenthal test was negative.

Apparently the Rosenthal test was not quite so sensitive as the Kahn test. The tendency to false positive reactions, as in all of the microprecipitation tests, seems to be slightly greater than with the Kahn test. It is frequently rather difficult to read the weakly or doubtfully positive reactions, but this is also true of the Kahn test.

COMPARISON VALUE OF TESTS

In determining the practical value of these tests, we may apply four criteria:

Specificity.—By specificity, we denote reliability and accuracy. The test must be sufficiently sensitive and yet not so sensitive as to give false positive reactions. The Kahn test,[9] in two international competitions in which rigid requirements were followed, proved the most sensitive and gave the smallest number of false positive reactions. It is unfortunate that the Kline and Hinton tests were not performed by their authors at these competitions. Apparently, from a reading of the literature, the Kline test closely approximates the Kahn test in specificity, though the number of false positive reactions seems to be somewhat higher. The Rosenthal test has not been given sufficient trial as yet to determine its ranking, although we believe that it should closely parallel the Kline test when performed by an expert.

Ease in Reading.—The Kline and the Rosenthal tests rank about equally in ease of reading, although in the Rosenthal test there are

9. Kahn, R. L.: (*a*) The League of Nations Conference on Laboratory Tests for Syphilis, J. A. M. A. **93**:351 (Aug. 3) 1929; (*b*) Considerations of Present Status of Serology of Syphilis, Arch. Dermat. & Syph. **26**:597 (Oct.) 1932.

numerous large aggregates of cholesterol or impurities which must be ignored in reading a test. These are not confusing, however, when the test has been performed many times. The Kahn test is somewhat more difficult to read, especially in the weaker reactions. The microscopic reactions seem to be more definite and more sharply demarcated than the tube tests.

Simplicity.—The use of special apparatus and materials detracts from the practicability of a test. In the matter of the preparation of antigen, the Kahn and Rosenthal tests are preferable, as it takes a good deal more trouble and time to prepare the antigen for the Kline test. The Kahn test requires the use of many pipets and tubes and preferably a shaking machine. A microscope is necessary for the Kline and Rosenthal tests. The Rosenthal test is the simplest to perform, the Kline test next and the Kahn test less so. The working emulsion for the Rosenthal test, being much more stable, requires less work.

Rapidity of Performance.—The Rosenthal test can be performed most quickly, only a few minutes being required to set it up, and it can be read immediately. Performance of the Kline test takes more time, since fresh working emulsion must be made up daily, and saline dilutions are required in setting up the test. The Kahn test takes the longest time of these tests.

Purposes of Usage.—The requirements for a test depend also on the clinical use which is to be made of the information obtained. The Kahn test is preferable when one wishes to have a carefully controlled, titrated test, and is especially valuable in following cases in which treatment is being administered, as variations in the strength of the reaction have some importance. For rapid and immediate diagnostic needs, the microscopic tests seem to be of most value. For emergency use, the Rosenthal test seems to be most valuable, allowance always being made, however, for the fact that no one test can exclude the diagnosis of syphilis, and that one is always taking a chance in relying on one quick reaction. For purposes of immediate diagnosis when clinical suspicions have been aroused, the rapid microscopic tests may be of considerable value.

Thus, in summing up the advantages and disadvantages of each test, the Kahn test has been thoroughly tested and is satisfactory, but it requires a good deal of apparatus and time to perform. The Hinton test seems to be a little more complicated and more sensitive to variations in methods than the Kahn test. The Kline test seems slightly more sensitive than the Kahn test; the end-results are definite and quite easily read, but the preparation of antigen and working emulsion is tedious and requires a number of pipets, as well as incubation. The Rosenthal test seems quite sensitive; the antigen is easily prepared and

keeps for months, the test is quickly set up, and the reading is not difficult except in the doubtful cases. The microprecipitation tests have the advantage of requiring only minute amounts of serum.

COMMENT

There has been a great deal of discussion concerning the relative value of the complement-fixation and the precipitation tests with many persons advising combinations of both tests. The interpretation of the results, especially of the weakly positive reactions, has also given rise to considerable comment.

Kline, in a review of 2,809 tests with his method, found an agreement with the clinical condition of patients in 94.9 per cent of cases. The Kahn test and the Wassermann test with Kahn antigen (noncholesterolized) agreed clinically in 95.2 per cent. The Wassermann test with an acetone-insoluble antigen showed a clinical agreement in 93.5 per cent. Although the percentage of agreement of the slide precipitation test with the condition of the patient was practically the same as that of the Kahn test and a sensitive Wassermann test, its disagreement was more frequently due to a positive reaction in nonsyphilitic serum, whereas the disagreement of the other tests was more frequently due to a negative reaction with syphilitic serum. It was apparent that the slide precipitation test as performed, although about as sensitive as the Wassermann and Kahn tests, did not equal them in specificity. Later, with a more sensitive acetone-insoluble antigen, a review of 9,000 cases showed 98.9 per cent clinical agreement and only 10 false positive reactions, the test ranking in specificity with the Wassermann and Kahn tests. The very sensitive test apparently proved of even more value in early cases of syphilis and in cases in which treatment was instituted late. Nagle and Willett [10] preferred the Kahn to the Hinton test. Ashby [11] devised an ingenious method of differentiating results which should be considered as positive by using a combination of a complement-fixation and a precipitation test. She believes that the reaction should be reported as positive if a serum that is negative by one method is 3 plus or stronger by another method, if a serum is 1 plus by one method and is 2 plus or stronger by the other method, or if it is 2 plus by one method and 1 plus or stronger by the other method. Reactions stronger than these are, of course, reported as positive. We do not believe that this method replaces clinical evaluation of the patient and examination of the spinal

10. Nagle, N., and Willett, J. C.: Comparative Study of Kahn and Hinton Reactions, Arch. Dermat. & Syph. **21**:836 (May) 1930.

11. Ashby, Winifred: Study of the Disparity in Parallel Serological Tests for Syphilis; Its Use to Increase the Sensitiveness of Serologic Examination, and a Titration Method for Evaluation of Technic, Am. J. Syph. **15**:102 (Jan.) 1931.

fluid in determining the presence or absence of syphilis, but it may be of value in some instances. Schwartz [12] found that active syphilitic invasion of the viscera, especially when associated with gummatous lesions, produces the greatest reagin response as measured in the blood stream. Taylor, Knapp and Oglesby [13] stated that they can do 2 precipitation tests (the Kahn test and the slide test of Kline and Young) with greater ease and economy and obtain more information than when a single complement-fixation procedure is followed, and they believe that the demand on their public health laboratory for assistance in the laboratory diagnosis and control of syphilis may be met most satisfactorily by the use of precipitation tests. Austin,[14] on the other hand, stated that the Hinton test might be substituted for the Kahn test but not for a sensitive carefully standardized Wassermann technic. In discussing precautions previous to blood transfusion, Levine [15] stated that the colloidal condition of the serum may be such as to give a precipitation reaction and not a complement-fixation reaction and vice versa. He believes that the donor's serum should be tested on at least three occasions, and by as many laboratory procedures as possible, that is, by at least one warm incubation, one cold incubation and one precipitation procedure. One set of tests should be performed immediately preceding the transfusion. Kolmer [16] recommended a combination of the complement-fixation and the precipitation tests. He deplored the emphasis placed on the simplicity of precipitation tests. He stated that at least two serologic diagnostic methods were recommended by the Second Laboratory Conference on the Serodiagnosis of Syphilis by the Health Organization of the League of Nations, held in Copenhagen in 1928. Becker [17] studied the Kahn precipitation test in comparison with the Kolmer complement-fixation test, and discussed the difficulties in their

12. Schwartz, S. C.: The Reagin Content of Serum in Various Manifestations of Syphilis, Am. J. Syph. **15**:387 (July) 1931.

13. Taylor, E.; Knapp, H. J., and Oglesby, M.: The Microscopic Slide Precipitation and Kahn Tests in Public Health Laboratory, Am. J. Syph. **15**:231 (April) 1931.

14. Austin, H. A.: A Comparative Study of 2,000 Hinton, Kahn and Wassermann Tests, J. Lab. & Clin. Med. **15**:994 (July) 1930.

15. Levine, B. S.: Rapid Precipitation Tests for Syphilis and Blood Transfusion, Am. J. Syph. **15**:81 (Jan.) 1931.

16. Kolmer, J. A.: Recent Developments in the Serology of Syphilis, Am. J. Syph. **15**:383 (July) 1931.

17. Becker, S. W.: (*a*) Comparison of the Kahn Precipitation Test and the Kolmer Complement-Fixation Test with Consideration of the Difficulties in the Diagnosis of So-Called Latent Syphilis, Am. J. Syph. **11**:131 (Jan.) 1927; (*b*) The Anticomplementary Reaction of Blood Serum to the Kolmer Complement-Fixation Test Controlled by the Reaction to the Kahn Precipitation Test, J. Lab. & Clin. Med. **12**:265 (Dec.) 1926.

interpretation, especially of weakly positive reactions, and the necessity for careful clinical control. He also performed the Kahn test on blood serums which were anticomplementary by the Kolmer test and found that the precipitation test is useful in determining the significance of anticomplementary reactions. McIntyre and Gilman [18] compared the Kolmer and the Kahn tests with careful control by clinical study and concluded that both the complement-fixation and precipitation tests should be performed on every serum. Miller [19] studied the Kline microscopic slide test, as compared with the Kolmer and the Kahn tests, and concluded that it is slightly more sensitive and also gives a higher percentage of false positive reactions. Heathman and Higginbotham [20] concluded that a combination of the Kolmer and Kline tests is better than the Kolmer or Kahn test. They state that the greater sensitivity of the Kline test outweighs the disadvantage of the tendency toward false positive reactions. Levine and Bromberg [21] studied the Eagle, Kahn and Kolmer tests and could not determine any marked advantage for the Eagle test.

CONCLUSIONS

On the basis of our performance of the Hinton tube precipitation test and the Kline and Rosenthal microscopic precipitation tests with careful clinical control, all three tests appear to be satisfactory. We do not believe that their advantages would justify substitution of one of them for the Kahn test, which is performed on all serums in our clinic. We believe that the Kolmer test gives information not obtainable by any precipitation test. On the other hand, the precipitation reaction will often be positive when the complement-fixation reaction is negative. The precipitation test is especially useful in cases in which the serum is anticomplementary by the complement-fixation test. It is not merely advisable, but imperative, that a complement-fixation test and a precipitation test should be performed on each serum.

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18. McIntyre, M. C., and Gilman, R. L.: A Clinical Comparison of the Kolmer Modification of the Wassermann Test and the Kahn Precipitation Test in Syphilitic and Nonsyphilitic Cases, Am. J. M. Sc. **176**:843 (Dec.) 1928; Serologic Studies: II. A Clinical Comparison of the Kolmer Complement Fixation and the Kahn Precipitation Test in Syphilitic and Nonsyphilitic Cases, J. A. M. A. **93**:358 (Aug. 3) 1929.

19. Miller, T. H.: The Kline Slide Precipitation Test for Syphilis, Am. J. Syph. **4**:583 (Oct.) 1929.

20. Heathman, L. S., and Higginbotham, Margaret: A Study of the Kolmer-Wassermann, Kahn and Kline Tests, Am. J. Syph. **16**:385, 1932.

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SENSITIZATION TESTS: THEIR VALUE IN DERMATOLOGY

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This report represents the result of an allergic study of certain cutaneous diseases over a period of four years. The investigation was carried out by a group of four physicians under the direction of Dr. Aaron Brown, assisted by Dr. Edgar B. Spiegel, Dr. Samuel Friedman and me. The cases were carefully chosen from the department of dermatology. In all, *262* patients were investigated. Because of the numerous visits that were required for a thorough study, only about 45 per cent of the patients were followed through completely.

A detailed and careful history was obtained in each case. This is without doubt the most important single factor in the proper study of a supposedly allergic person. A standard set of about sixty printed questions was used, in addition to which special questions were asked according to circumstances.

METHODS OF TESTING

The following technics were used:

1. *Dermal or Scratch Method.*—A superficial linear scratch, ⅛ inch (0.32 cm.) in length was made in the skin without drawing blood. The suspected material, usually in powder form, was moistened with tenth-normal sodium hydroxide and gently rubbed into the scratch. A positive reaction consisting of an urticarial wheal on an erythematous base was obtained within from ten to thirty minutes. Another scratch to which alkali alone was added was used as a control.

2. *Intradermal Method.*—Two-hundredths cubic centimeter of a proper dilution of an extract of protein was injected intradermally, and the reaction was read after from twenty to thirty minutes. Depending on the size of the wheal, pseudopods and erythematous base, the reactions were classified as negative, slight, moderate and marked, or as —, +, ++ and +++.

3. *Indirect or Passive Transfer Test.*—Five-hundredths cubic centimeter of the sterile serum of a patient was injected into the skin of a nonallergic person at several sites which were tested dermally or intradermally forty-eight hours later. Tests with the same substances were made in control sites, 2 inches (5 cm.) to the side of the prepared sites. Reactions were read and recorded in the same manner as with the direct testing, except that they were compared with the controls. A reaction was considered positive if the wheal in the sensitized area was larger than the control and if it itched and had an erythematous base. This is the

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Prausnitz and Küstner test,[1] which was reserved for special situations: (*a*) for small children in whom direct testing was difficult; (*b*) for children or adults who suffered from generalized eruptions and who presented no healthy skin for direct testing, and (*c*) experimentally and diagnostically, to demonstrate specific antibodies (reagins) in the circulating blood of an allergic person.

4. *Patch Test.*—This consisted in applying the suspected substance (preferably in solution) to an untraumatized or slightly traumatized area in the skin and permitting it to remain for twenty-four hours or more. If the test substance was an insoluble solid, it was crushed to a powder and covered with a small piece of white blotting paper, saturated with a buffer saline (Coca's fluid) and held in place by a square of adhesive (from 6 to 8 cm.), the center of which was covered with a square of cellophane or other impervious material. In the case of a liquid, the blotting paper was simply saturated with it and held in place. Depending on the irritability of the substance, but more on the sensitivity of the patient, a positive reaction was obtained after from a few hours to a few days (at times seven days or more). A reaction was considered positive if there was a patch of dermatitis of varying severity at the test site, accompanied frequently by a flare-up of an existing residual dermatitis in distant parts. The concentration of a substance to be tested should be such that it is not an irrtant to the normal skin. That was best accomplished by using high dilutions and comparing positive reactions with control patch tests performed with the same dilutions on a normal person.

Objectively and biologically, this type of reaction is totally different from that producing an urticarial wheal. Its pathogenesis is not clearly understood. Bloch[2] offered the following theoretical explanation: In the former the cells of the epidermis are the probable seats of sensitivity, while in the latter the capillaries of the skin are involved.

The great majority of tests were performed by the intradermal method (urticarial reaction); I think that this is more reliable than the scratch method, and when it is properly performed, it is free from danger. The materials for tests were obtained from the New York Hospital and were prepared according to the method of Coca.[3] To insure uniformity of interpretation, reactions were invariably read by the tester and by one or all of the other members of the staff. Only moderate or marked reactions were recorded as positive, while slight or delayed reactions were with few exceptions recorded as negative. The usual number of proteins employed was 105. They consisted of the commonest animal danders, pollens and other inhalants, a representative group of the cereals, flour, meat, sea food, vegetables, spices, fruit, egg and milk.

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Retests after both positive and negative reactions were performed in many cases, especially in those in which the history suggested sensitivity, though the reactions were negative. They were also performed in cases in which the patients gave positive reactions, but when the ingestion or contact of the substances did not aggravate the eruption. With few exceptions the original positive reactions were sustained on retesting. Findings which were reversed on retesting affected only the general number of positive and negative reactions, but in no instance were they of etiologic significance.

The total number of tests performed by more than one method was 12,600. Ninety-nine patients with an average of fifteen visits received from 75 to 105 tests. Forty-three patients with an average of eight visits were given from 35 to 70 tests, and the remaining 120 patients, with an average of from one to five visits received from 0 to 35 tests.

Of the total of 12,600 tests, 12,486 were performed intradermally, of which 1,199 were positive and 11,287 negative. In addition, 114 patch tests were performed, 38 of which were positive and 76, negative. Eighty-six positive intradermal tests were checked by means of the passive transfer method (Prausnitz-Küstner [1]), 37 remaining positive and 49 proving to be negative.

External treatment and desensitization therapy for associated allergies were given to most of the patients; some of them received internal medication in addition. This was necessary not only to relieve subjective symptoms, but also to gain the patients' confidence and to aid in securing regular attendance. To complete the entire list of 105 tests, from ten to fifteen visits were necessary. For further observation and follow-up, additional visits were required, which accounted largely for the failure of slightly more than half of the total number of patients to cooperate fully.

PRACTICAL RESULTS

The diseases included in this study were chiefly eczema, urticaria and dermatitis venenata (over 80 per cent of the cases); others were prurigo, erythema multiforme, angioneurotic edema and neurodermatitis. Details regarding the number of tests and reactions are given in table 1.

ECZEMA

There were 86 cases of eczema, in 25 of which there was a family history, and in 20 a personal history, of allergy (chiefly asthma and hay fever). Five patients had both a family and a personal history of allergy.

Of the 86 patients only 1 was clinically cured; 8 were markedly improved, 20 improved and 2 unimproved. In 55 cases the final results could not be ascertained.

In the case of the patient who was clinically cured, the etiology was definitely determined. It was due to contact with silk and feathers, to which the patient had given markedly positive reactions on intradermal testing. She had also reacted positively to eleven other substances, but they were of no significance.

The cause was only partially demonstrated in the 8 patients who showed improvement. The substances to which the patients reacted positively played a rôle in the etiology. Each patient gave more than one positive reaction and reacted to more than one class of protein. While it was evident that the substances causing positive reactions were not the immediate and exciting causative agents, the avoidance of them nevertheless seemed to have a favorable effect on the eruption. Final improvement was obtained only after various local and constitutional measures had been instituted.

TABLE 1.—*Total Number of Patients Tested and Their Corresponding Reactions*

Clinical Diagnosis	Number of Cases	Number of Intradermal Tests		Number of Patch Tests		Total Number of Reactions		Number of Tests Performed, Total
		Positive	Negative	Positive	Negative	Positive	Negative	
Eczema	86	461	3,395	8	26	469	3,421	3,890
Urticaria	86	482	5,024	4	14	486	5,038	5,424
Dermatitis	42	76	934	26	36	102	970	1,072
Prurigo mitis	20	39	562	0	0	39	562	601
Angioneurotic edema	10	83	571	0	0	83	571	654
Erythema multiforme	15	38	627	0	0	38	627	665
Neurodermatitis	3	20	174	0	0	20	174	194
	262	1,199	11,297	38	76	1,237	11,363	12,600

The tests failed to show the cause of the eruption in any of the 20 patients classed as improved. Collectively, the patients gave a large number of positive reactions, but the ingestion or avoidance of the foods had no effect on the disease. Improvement was due solely to local and general treatment.

Two patients failed to improve when given a restricted diet (indicated by the tests) and local treatments; and they were referred back to the clinic for cutaneous diseases.

The final results in 55 cases were unknown. Each of the patients had given some positive reactions to food proteins. Each was treated locally and instructed to avoid substances to which he reacted positively. A goodly number of the patients were under observation for from two to ten weeks. At their last visit, most of them were unimproved, though a few were slightly benefited. They represented the large number of patients who failed to cooperate fully.

It is interesting to note that, while milk, egg and wheat are commonly believed to be the most frequent offenders in eczema due to food (specific eczema), this had not been the case in our study. None

of the aforementioned foods was definitely responsible for a case of eczema—though collectively the foods produced positive reactions twenty-eight times—nor gave the largest number of positive reactions. A partial list of substances which gave the most frequent intradermal reactions in eczema is as follows: house dust, nineteen; chicken meat, sixteen; cheese, turnip and wheat, each twelve; banana and tomato, each eleven; feathers, ten; milk and shell-fish, each nine; beef, egg, parsnip and pork, each seven; chocolate and sweet corn, each six; lima bean and sweet potato, each five.

REPORT OF CASES

CASE 1.—*Clinically cured. Silk and feathers demonstrated as cause.*

E. M., a school girl, aged 12, with no family history of allergy, presented an erythematosquamous eczema of the face, neck chest and parts of the extremities, which had persisted with slight remissions since she was 2 years old. From 2 to 9 years of age she had suffered from violent attacks of asthma, which had no relation to the season and no special effect on the eczema. For the three years previous she had suffered from attacks of late hay fever which appeared from the middle of August to the onset of cold weather. She had received treatment only for the eruption, with little benefit. No etiologic factors could be elicited from the history.

She was tested completely and found to give positive raections to: beet, clam, crab, feathers, halibut, house dust, lobster, oyster, scallop, shrimp, turnip and watermelon. The avoidance of foods to which she reacted positively had no effect on the eruption. She recovered after eleven months of local treatment and strict avoidance of silk and feathers.

CASE 2.—*Markedly improved. Suggestive cause demonstrated.*

J. Y., a male infant, aged 1 year, had suffered from generalized eczema since the age of 2 months. During the first seven months the eruption was limited to the face. Later it became generalized. The maternal grandmother had suffered from asthma. The personal history was unimportant.

The patient was breast fed up to the age of 3 months. He was given a formula of cow's milk and dextri-maltose. Orange juice was begun at the age of 6 weeks. Cereals were added to the diet at the age of 6 months. Vegetables and occasionally fruits, especially banana, were first begun at the age of 6½ months. He had been given no eggs. His mother believed that when cereals were omitted from the diet the eruption improved.

On direct testing he gave positive reactions to: asparagus, banana, beef, egg, lima bean, cow's milk, orange, potato, rye, spinach, string-bean and wheat. On passive transfer (Prausnitz-Küstner method) reactions were positive to: asparagus, banana, egg, lime bean, potato, spinach and string-bean.

Marked improvement followed after four months, when he was placed on the following diet and medication: butter, carrot, lettuce, cow's milk boiled for twenty minutes, oatmeal, rice and tomato. He was given viosterol, 10 drops three times a day, and a medicated [4] paste was applied locally. The avoidance of the foods to which he gave positive reactions on passive transfer and the boiling of the milk for twenty minutes undoubtedly contributed toward the improvement.

4. The following paste was used: salicylic acid, 2 Gm.; starch, 8 Gm.; ointment of zinc oxide, 90 Gm. The ointment of zinc oxide consisted of: zinc oxide, 20 Gm.; petrolatum, 80 Gm.

An interesting feature was shown by his mother, who acted as a substitute for the passive transfer. Once, when her arm was sensitized with the child's serum in eight sites, she had eaten a banana. Within from one to two hours all of the sensitized sites showed large urticarial wheals, which represented markedly positive reaction to banana. She had never been subject to urticaria, and there were no urticarial wheals elsewhere on her body at the time.

CASE 3.—*Improved. Cause not demonstrated.*

A man, a Puerto Rican, aged 38, with no family or personal history of allergy, presented erythematosquamous patches of eczema on the dorsal surface of the hands and feet and on the lower third of the legs, from which he had suffered for seven months. He had worked for the preceding three years in a chocolate factory. He said that he had had no contact with irritants other than the usual domestic and factory substances. He was unable to account for an etiologic factor except that during the past two weeks, when he had not worked, the eruption had somewhat subsided.

He was tested completely and gave a positive reaction to: banana, blue fish, cantaloup, chicken meat, fig, house dust, lima bean, lobster, parsnip, prune, rice, salmon, sardine, tomato and turnip. A patch test for chocolate which he handled gave a negative reaction. An intradermal test of chocolate was also negative. Ingestion or omission of foods to which he gave a positive reaction had no influence on the eruption. The patient improved at the end of four months, apparently from local treatment with ointments.

URTICARIA

Of the 86 patients with urticaria who were studied, 15 gave an allergic family history, 26 an allergic personal history and 7 a combination of both types.

Of the 86 patients, 3 were clinically cured, 28 were improved, and 2 were unimproved. The final results in 53 cases were not known.

The cause of the disease was definitely demonstrated in 3 cases. In 1 case it was contact with silk; in another, ingestion of cabbage, and in a third, ingestion of acetylsalicylic acid.

The cause was suggested in 28 cases in which the patients improved. They reacted to more than 1 protein or class of proteins. So long as they strictly abstained from all of the substances to which they had given positive reactions, attacks of urticaria were milder and much less frequent. Carelessness in diet seemed to increase the frequency of relapses. The exact rôle which the substances causing a positive reaction played in precipitating the attacks was not determined. Whether they were the exciting agents or simply contributory factors or whether they played some as yet unrecognized part cannot be stated. Nor was it ascertained which of these substances, singly or collectively, played any of the aforementioned rôles.

In the case of the 2 patients who were not improved and of the 53 patients in whom the final results were not known, little else can be stated. Collectively they gave a great number of positive reactions. One must assume that this group of patients adhered to their diets as diligently as any of the others. The only inference, therefore, that one

can draw is that in the 2 patients who did not improve the positive findings were definitely of no etiologic significance. Of what significance they were in the 53 cases of unknown cause obviously cannot be stated.

The foods commonly believed to be the most frequent causes of allergic dermatoses did not prove to be so in my study of urticaria, as was true in my case of eczema. They were not even among those which gave the most frequent reactions, as shown in the following list: house dust, twenty-six; turnips, seventeen; beef and tomato, each sixteen; chicken meat and feathers, each twelve; banana, cheese and onion, each ten; Brussels sprout, lima bean and mushroom, each seven; salmon and sweet potato, each six; asparagus and sea food, each five; wheat, four; egg and milk, each two; orange, none.

CASE 4.—*Clinically cured. Cause (contact with silk) demonstrated.*

A. R., a woman, aged 31, married, complained of frequent attacks of hives, chiefly on the neck and chest, of one year's duration. Attacks appeared every few weeks, lasting from one to three days, and invariably followed the wearing of certain silk apparel, especially dresses. A silk scarf and a piece of one of her silk dresses were applied to her neck and wrist, respectively, and by the end of two minutes had caused marked redness and unbearable itching, requiring their removal. The same silks applied to the skin of a normal person as control caused no reaction. She was also tested with twelve suspected food proteins, but gave a negative reaction to all of them.

CASE 5.—*Improved. Cause not demonstrated.*

R. S., an office clerk, aged 21, became subject to attacks of generalized urticaria, associated with angioneurotic edema, affecting the eyelids and dorsal surface of both hands. Attacks first began ten months previously. Their duration varied from a few days to two weeks. She had from six to eight relapses. Modified diets did not seem to be of benefit. There was nothing in the history to suggest possible causation except that attacks appeared when she was nervous.

She was completely tested and found to give positive reactions to cat epidermis, chicken meat, feathers, house dust, parsnip, spinach and tea.

She made an earnest attempt to avoid all of the foods to which she gave a positive reaction. In addition she received ephedrine sulphate and calcium lactate internally. After four months she felt considerably improved, but was still subject to mild relapses.

CASE 6.—*Unimproved. Cause not demonstrated.*

C. S., a carpenter, aged 34, had suffered from generalized urticaria for eight months. There was no family or personal history of allergy. No cause was suggested on detailed questioning. Skin tests showed positive reactions to clam, crab, egg, feathers, house dust, lobster, milk, oatmeal, oyster, salmon, scallop and shrimp. He was treated intensively with alkalis, cathartics, ephedrine sulphate internally and antipruritic substances externally for nine months with no improvement. He avoided all of the substances to which he had reacted positively. On returning for observation, six months after the last treatment, he stated that he was still subject to frequent attacks.

DERMATITIS VENENATA

Under the heading of dermatitis venenata were included cases thought to be due to external irritants of occupational or other origin.

Intradermal tests were found to be of no value in these cases, though decided assistance was afforded by patch tests. Indeed, owing to the latter method of testing, the results obtained in this group of patients were more gratifying than those in any of the others. There were 42 patients, 9 of whom gave a family and 5 a personal history of allergic conditions. In 3 cases both types of allergy had been present.

Eight patients in this group were clinically cured, and 6 were improved, while in the remaining 28 the results were not ascertained.

In the 8 clinically cured patients, the etiology was definitely demonstrated. In 3 cases, the cause was a hair lotion; in 2, poison ivy, and in 1 each, tar soap, shoe polish and ragweed oil.

In 6 patients classed as improved, the cause was suggestively demonstrated. Each patient gave a number of positive reactions to intradermal tests with foods and one or more positive reactions to patch tests with substances with which they had come in contact.

The ingestion of foods to which they showed positive reactions did not seem to influence the eruption. Improvement, however, invariably followed when the patients remained away from their respective occupations (contact).

In the remaining 28 patients the final results were not known. Collectively they gave a number of positive reactions to intradermal tests with food proteins and a number of positive reactions to patch tests with substances with which they had come in contact. It was definitely ascertained that the ingestion or avoidance of foods to which the patients gave a positive reaction had no effect on the eruption. The effect of avoiding contact with substances to which they had given a positive reaction with the patch test unfortunately could not be learned, as the patients did not remain long enough under observation.

CASE 7.—*Clinically cured. Cause (hair lotion) proved.*

S.M., a woman, a dress finisher, aged 25, presented an acute papular dermatitis on the face, neck, chest and both arms, of one week's duration. Two weeks prior to the onset of the eruption she began using Kay's Hair Color Restorer. A few hours following the fourth application of the hair lotion, a mild dermatitis appeared on the face, which rapidly spread to other parts of the body. With further use of the hair lotion, the dermatitis was very much aggravated. A patch test with that solution was markedly positive after twenty-four hours (a large bulla appeared on an erythematous base). With the use of soothing lotions externally and the strict avoidance of the hair lotion, the hat and all of the clothing she wore while she was afflicted, she was entirely well at the end of eight weeks.

CASE 8.—*Improved. Cause suggestively demonstrated.*

I.W., aged 53, a shoe repairer, presented an erythematosquamous dermatitis of the chest, forearms and hands of six months' duration. The eruption occurred during the warm months and disappeared with the onset of cold weather. He had worked at this trade for fourteen years. He said that he had not had contact with irritants other than the usual substances that he handled. On routine intradermal

testing he gave positive reactions to house dust, leather dust and veal. A patch test with "liquid wax" was strongly positive at the end of seven days. By applying soothing local treatments and staying away from work, he was much improved at the end of three weeks.

PRURIGO MITIS

In prurigo mitis, as in dermatitis venenata, intradermal testing with food proteins was found to be of no value. Of the 20 patients who were studied, 4 gave a family history of allergy. Their personal histories were negative for allergic conditions. Of the 20 patients, 3 were improved by local or general measures and avoidance of overexposure to sunlight. Avoidance of foods to which they gave a positive reaction had no influence on their eruptions. The final results in the remaining 17 cases were unknown, the patients remaining under observation from two weeks to five months.

CASE 9.—*Improved. Cause not demonstrated.*

P. W., a school boy, aged 13, presented a discrete, intensely itchy, papular eruption of the forehead and extensor surfaces of the extremities. Attacks began at about the age of 1 year. The eruption would develop suddenly during the early spring, persist throughout the entire summer and disappear with the onset of cold weather. Attacks appeared and disappeared with equal regularity every year. The history did not suggest any causative factors, except that the eruption seemed to be decidedly worse on overexposure to sunlight.

He was tested completely and gave positive reactions to: almond, banana, beef, cauliflower, cherry, chicken meat, crab meat, peach and spinach. He remained under observation for five months. The avoidance of the foods to which he gave a positive reaction did not seem to be of benefit. On avoidance of overexposure to sunlight and with the onset of cold weather, the eruption spontaneously disappeared.

ERYTHEMA MULTIFORME

Fifteen cases of erythema multiforme were studied, including 6 of the bullous type. Only 3 patients gave a family history and 1 a personal history of allergic conditions.

Intradermal tests proved futile in an attempt to determine the causative factors (except perhaps in 1 case). Few positive reactions were obtained, and these had no etiologic significance. Four patients improved somewhat after abstaining from substances to which they gave positive reactions, though relapses still occurred. In 1 case there were positive reactions to banana and chicken meat on passive transfer (Prausnitz-Küstner method). Avoidance of these foods seemed to be of decided benefit. The patient previously had recurring attacks every two or three months, but after abstaining from the aforementioned foods, he remained well during nine months of observation. The remaining 11 patients failed to improve. The relapses continued to be as frequent and as severe as before. The patients remained under observation for periods varying from three weeks to a year and a half.

ANGIONEUROTIC EDEMA

The demonstration of causative factors by intradermal tests proved to be as disappointing in angioneurotic edema as in urticaria. While a greater number of positive reactions were obtained in angioneurotic edema than in urticaria, they did not seem to have any greater significance, though a few patients apparently improved on the avoidance of substances to which they gave positive reactions. The cause was not definitely determined in any case.

Ten cases were studied. Two patients gave a family history and 4 a personal history of allergic conditions. In 4 patients the cause was at least suggested. In 1 patient who was subject to hay fever, treatment with an aqueous extract of ragweed pollen seemed to improve the eruption. In 3 cases, strict avoidance of foods to which the patient gave a positive reaction appeared to be of benefit. The patients remained under observation for from two to eighteen months. The results in the remaining 6 cases were unknown.

CASE 10.—*Improved. Cause suggestively demonstrated.*

E. W., a woman, aged 35, a telephone operator, became subject to attacks of angioneurotic edema six months previous to presentation for treatment. The first attack consisted of a sudden sensation of choking in the throat and chest, which was soon followed by the appearance of lumps on the dorsal surface of both hands and a bilateral swelling of the eyelids. The attack lasted from two to four hours. About two months later, the patient suffered a similar relapse which lasted twenty-four hours. The last attack occurred three weeks before admission. The family and personal histories showed no other forms of allergy.

There was nothing in the history that was definitely suggestive of etiologic factors, except that the last seizure developed almost immediately after the ingestion of a piece of raisin pie and a glass of grape juice.

She was completely tested and found positive to: apricot, banana, beet, brussels sprouts, buckwheat, cabbage, cantaloup, carrot, cauliflower, celery, chicken meat, cornmeal, coffee, lettuce, orange, prune, raisin, rice, rye, string-bean and sweet corn. She was retested with every one of these foods, and the original findings were sustained. On strict avoidance of all of these foods, she was free from attacks during the five months that she was under observation.

Dermographism, frequently present in angioneurotic edema, was successfully demonstrated by passive transfer. A narrow band, 3 inches (7.6 cm.) in length, was sensitized with the serum of a patient subject to marked dermographism. Gentle stroking of the sensitized area produced typical dermographism, while similar stroking of the skin 2 inches (5 cm.) from the sensitized area failed to provoke this response.

NEURODERMATITIS

The determination of etiologic factors by means of intradermal tests was a failure in 3 of the patients studied. Although the average number

of positive reactions for each patient was even higher than in cases of eczema or dermatitis venenata, the avoidance of foods to which the patient gave a positive reaction did not influence the course of the eruption. Patch tests were not performed, as the histories did not suggest irritation due to external substances. The number of cases was obviously too small from which to draw conclusions. All of the patients improved under local treatment, remaining under observation for from two to four months. None of them had a family history of allergy. One patient had a personal history of asthma.

TABLE. 2—*Etiologic Demonstration and End-Results Based on Positive Cutaneous* Tests in 262 Patients with Various Dermatoses*

Total No. of Cases	Clinical Diagnosis	Average No. of Positive Reactions per Patient	Clinically Cured, Cause Demonstrated		Improved, Cause Suggestively Demonstrated		Improved, Cause Not Demonstrated		Unimproved, Cause Not Demonstrated		Results Unknown	
			No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
86	Eczema.....	5.4	1	1.1	8	9.3	20	23.6	2	2.3	55	63.9
86†	Urticaria.....	5.6	3	3.4	28	32.4	0	0	2	2.3	53	61.1
42‡	Dermatitis venenata..	2.5	8	19.0	6	14.2	0	0	0	0	28	63.7
20	Prurigo mitis.....	1.9	0	0	0	0	3	15.0	0	0	17	85.0
15	Erythema multforme	2.5	0	0	4	26.6	0	0	11	73.4	0	0
10	Angioneurotic edema	8.3	0	0	4	40.0	0	0	0	0	6	60.0
3	Neurodermatitis.....	6.6	0	0	0	0	3	100	0	0	0	0

* Mainly intradermal tests.

† Intradermal tests demonstrated the cause in one case; a patch test proved the cause in another, and in the third, in which the patient was clinically cured, the cause was determined by a proper history and follow-up.

‡ Good results were due to elimination of irritants, as demonstrated by patch tests.

COMMENT

Of late years the subject of allergy has been intensively studied and has been the cause of much optimism and enthusiasm. Immunologists have definitely solved much of the mystery of hay fever and asthma. They have demonstrated that the conjunctiva and the mucous membrane of the nose, throat, bronchi and gastro-intestinal tract are shock organs and are capable of producing certain symptoms when in contact with a sufficient amount of antigen to which they are sensitive. Positive reactions to pollens, food and other substances were found to be specific and diagnostic in both asthma and hay fever. The skin was then included as a shock organ in the human system, and the seed of difficulty was planted.

There are indications that the skin is a shock organ. Dermatoses on an allergic base have been demonstrated. However, such instances are not nearly so frequent as allergic manifestations affecting the mucous membranes and by no means as common as some enthusiasts believe.

A diagnosis in allergy is based on four cardinal principles, usually more than one principle operating in a particular case: 1. Contact: a history of attacks of a morbid process on contact with a suspected substance. 2. Removal: the disappearance of symptoms on the avoidance of the substance. 3. Tests by injection or ingestion: the production of symptoms on the injection (of pollens in hay fever) or ingestion (of foods in specific dermatoses). 4. Therapeutic injections: the relief of symptoms by the injection of increasing amounts of an extract of the substance to which the person has been found sensitive (desensitization).

It is evident, therefore, *that the mere finding of a positive reaction to some substance with any method of cutaneous testing is of no diagnostic significance unless the aforementioned principles are demonstrated.* The frequency of such demonstrations with positive immediate reactions to pollens in hay fever is only too well known. Such, however, is not the case with similar reactions to food proteins in dermatoses.

Another very important factor that is overlooked by the unwary is the fact that diseases like urticaria, angioneurotic edema and erythema multiforme (commonly considered allergic) are usually transitory or self limited, and that eczema (also considered allergic) has frequent remissions. Irrespective of what is being ingested or avoided, the eruptions may disappear spontaneously and recur at a later period. Such remissions are apt to be designated as cures and attributed to the avoidance of substances to which the patients reacted positively.

These so-called allergic dermatoses are a purely dermatologic problem, and the factors constituting their etiology are many. They include disturbances in the vascular system, changes in the chemistry of the blood and skin, the neurogenic status, faulty metabolism, focal infection, endocrine dysfunction and probably some other as yet undetermined factors which only time and further study will bring to light. To consider a positive cutaneous reaction in these diseases of paramount diagnostic importance not only would be contrary to the accepted principles of immunology but would show a disregard for established clinical dermatologic evidence.

SUMMARY

A series of 262 cases of various dermatoses was studied over a period of four years by a group of four men well acquainted with the theoretical and practical phases of immunology. The dermatoses included eczema, urticaria and dermatitis venenata (80 per cent of the cases) and also prurigo, erythema multiforme, angioneurotic edema and neurodermatitis. The cases selected were those in which an allergic cause

was suspected. The study was made by taking careful histories and performing intradermal tests and a few patch and passive transfer tests. A total of 12,600 tests were performed, of which 1,237 were positive and 11,287 negative. Of the total number of 12,600 tests, 12,486 were performed intradermally, of which 1,199 were positive and 11,287 negative; 114 tests were performed by the patch method, of which 38 were positive and 76 negative. Eighty-four positive intradermal tests were checked by means of the passive transfer method; of these 36 remained positive, and 50 proved to be negative. Only those to which the patient gave moderate or marked reactions were classed as positive. A little less than half of the cases could be followed for complete study. Sufficient data were obtained, however, to draw the following conclusions.

1. Intradermal tests are of little value in demonstrating the cause of cutaneous diseases.

2. A great number of positive intradermal reactions are obtained, but they are rarely of practical significance.

3. Positive reactions to food substances or inhalants administered intradermally in patients with cutaneous diseases are far less specific than similar reactions to pollens in patients with hay fever.

4. The indiscriminate subjection of patients with dermatoses to a large number of skin tests is not justifiable. Far greater etiologic help can be obtained by securing a proper history and making a correct dermatologic survey.

5. Patch tests are of decided value, especially in cutaneous diseases which are due to external irritants.

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XERODERMA PIGMENTOSUM

A STUDY IN SENSITIVITY TO LIGHT

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Xeroderma pigmentosum possesses such striking characteristics and is so well known to dermatologists that no description of the disease is required. Its hereditary tendency is well known; it acts as a recessive characteristic with no tendency toward sex differences. Consanguinity of the parents has been recorded in from 17 to 59 per cent of the cases, and was regarded by Toyama as the reason for the high incidence in Japan.

The course of this disease is progressive, the exposed parts of the skin undergoing all of the progressive changes of senility; as a rule, death results from carcinomatosis. Kaposi described the condition in detail, but apparently failed to notice its frequent onset as an acute erythematous reaction to solar exposure. His denial of photosensitivity as a factor in the production of the changes found in xeroderma pigmentosum led to a delay in arriving at an understanding of the pathogenesis. Ephelides, seaman's or farmer's skin and senile skin are all characterized by the same lesions and produced by the same external agents, and some observers have regarded them as early forms of xeroderma pigmentosum. The late changes closely resemble roentgen-ray dermatitis clinically.

There are a great number of diseases related to sensitivity to light; some are regarded as true sensitizations while others have a less direct relationship. Xeroderma pigmentosum, hydroa vacciniforme or aestivale, prurigo aestivalis, eczema solare and urticaria solaris are usually regarded as true sensitizations. Hausmann and Haxthausen [1] grouped the pruriginous and eczematous eruptions and believe that there is no sharp division between them.

That a number of drugs are capable of evoking a sensitization to light in living organisms was demonstrated by Tappeiner in 1899 (eosin, methylthionine chloride, U. S. P. [methylene blue] and acridine). Hausmann reported similar effects from hematoporphyrin. In

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1. Hausmann, W., and Haxthausen, H.: Die Lichterkrankungen der Haut, Strahlentherapie, Sonderbände, Berlin, Urban & Schwarzenberg, 1929, vol. 11.

a group of patients being treated for gonorrhea, Jausion observed a number of cases of sensitivity to light, and he proceeded to demonstrate that the sensitivity resulted from the use of acriflavine hydrochloride, which is a drug of the acridine group. Haxthausen observed a patient with psoriasis who exhibited sensitivity to sunlight, but not to ultraviolet radiation, following the use of acriflavine hydrochloride. The barbitals are capable of disturbing hematoporphyrin metabolism, and occasionally produce sensitivity to light (sulphonmethane, sulphonethylmethane, phenobarbital). Argyria is often more marked on the exposed parts.

A number of cutaneous eruptions are precipitated by exposure to sunlight, appear only on exposed parts or are made worse by continued exposure: Lupus erythematosus and pellagra come closest to being accepted as true sensitizations. Some cases of lichen planus, acne vulgaris, rosacea, eczema and erythema multiforme are apparently made worse by light. Rubeola, varicella and vaccinia have been observed to appear earlier, produce a more intense reaction and involute more quickly on irradiated areas. The Pirquet and Schick tests, when applied to previously irradiated areas free from erythema, evoke a more intense reaction than is normal. Kreibich described a condition resembling scleroderma which followed exposure to sunlight.

The effect of light on the production of carcinoma of the skin was suggested by Unna and others, and recent experimental studies tend to substantiate their belief. There is an increase in the cholesterol and the cholesterol ester content of the skin after ultraviolet irradiation, and there is probably a relationship between this observation and the high cholesterol content of carcinomas of the skin.

The color, thickness, fat content and temperature of the skin all influence its reaction to irradiation. Active hyperemia increases the local sensitivity, and anemia has the opposite effect. A number of other factors which influence this reaction were reviewed recently by Ellinger.[2] He found seasonal variation in the same persons, the greatest sensitivity appearing in the spring and fall; females were found to be less sensitive than males and brunettes less than blonds. There was, as a rule, an increase in sensitivity during menstruation, but this was not constant. After the third month of pregnancy sensitivity was increased. Racial differences seemed to depend on factors of complexion more than on any specificity of racial reaction. Sensitivity diminishes with advancing age, while from a clinical standpoint the changes in seaman's, farmer's or senile skin, though beginning before the age of 50, progress more rapidly and reach their height of development in later years.

2. Ellinger, F.: Die Lichtempfindlichkeit der menschlichen Haut, Strahlentherapie **44**:1, 1932.

THE EFFECTS OF RADIATION

The presence of radiations other than visible light has been known for many years. The infra-red and ultraviolet rays were discovered about 1800 by Herschel and Ritter, and the so-called chemical action of light rays was recognized by Charcot in 1859. In 1820 Home demonstrated the duality of the heat and light reactions evoked by sunlight, and Hammer in 1891 recognized the erythema of the latter by its latent period. In 1899 Finsen realized that the light reaction was produced by ultraviolet radiation as distinguished from visible light, and he applied this knowledge to therapeutic procedures. Not until the work of Freund in 1912 was the dividing line between these groups of radiations recognized. He used color filters and showed that light passing through a blue filter was capable of producing both types of reaction. No accurate measurements of the radiations involved were made until 1921.

Before discussing the measurement of these radiations it may be well to become oriented in the spectral field. One must first decide on a unit of measurement; the denomination most commonly used in this field is the millimicron:

1 millimeter = 1,000 microns
= 1,000,000 millimicrons
= 10,000,000 angstroms

The visible spectrum includes radiations with wavelengths from 750 to 380 millimicrons. Ultraviolet radiations include wavelengths between 380 and 60 millimicrons. Grenz or Bucky rays are in the region from 0.2 to 0.1 millimicron. Roentgen and gamma radiations have wavelengths extending down to 0.01 angstrom.

The two sources of light with which one is concerned in this study are the sun and the mercury vapor arc lamp. Dorno carried out extensive investigations of the solar radiations which actually reach the earth at Davos. There are, of course, variations depending on altitude and atmospheric conditions, but it is known that rays with a wavelength of 290 millimicrons or less rarely reach the earth's surface. He showed that even in the summer months (May to September) radiations of from 298 to 302 millimicrons penetrated only during the hours between 8 a. m. and 4 p. m. Even during these months such radiations form only a small part of the total. On March 5, June 15 and September 15 he found that rays with a wavelength of 300 millimicrons amounted to only 0.2, 1.2 and 0.4 per cent, respectively, of the number with a wavelength of 320 millimicrons.

In recent years there have been many studies on the production of erythema with reference to the measurement of radiations which are capable of producing such a reaction. Hausser and Vahle in 1921 and

1927, and Coblentz [3] and others in 1931, made careful measurements of the radiations which produce erythema on "normal" skin. Much of the difficulty in determining the exact limits depends on inability to secure sources of light emitting a continuous spectrum of uniform intensity. As a source of radiation Coblentz used a large mercury vapor arc in quartz, projecting the rays through a quartz prism, thus producing a spectrum. Experiments with such an apparatus on patients sensitive to light would be of great interest.

In these tests the erythema reaction was shown to be produced almost entirely by radiations of shorter wavelengths than 315 millimicrons. Freund claimed erythema-producing powers for radiations up to 340 millimicrons; Coblentz, for radiations up to 360 millimicrons in one case, and Reyn, for radiations over 400 millimicrons with very long exposures. From a practical standpoint, it may be assumed that the production of erythema begins at wavelengths of 315 millimicrons, reaches a maximum around 300 millimicrons and diminishes again to a minimum at about 280 millimicrons. Most workers observe a second maximum around 250 millimicrons; the height of this maximum varies with different observers. It is well known that the erythemas produced by different radiations differ qualitatively as well as quantitatively. It has been pointed out that long overexposure with rays of about 240 millimicrons produces only a slight reaction which may result in scaling, while at 313 millimicrons only a short overexposure produces vesiculation. The erythema also differs in color when produced by different groups of radiations. In general, it has been assumed that production of pigment depends on previous production of erythema; although this is the usual observation, it is known that longer radiations produce pigmentation without apparent production of erythema.

The mechanism of production of erythema is not well understood. Perhaps the most generally accepted theory is that of Sir Thomas Lewis, who believes that a histamine-like substance is liberated in the skin as a result of a photochemical process following exposure to the proper rays. There has been much experimental work done in this field, but as yet his explanation must be regarded as theory and not as proved fact.

PHOTOSENSITIVITY

In a recent general discussion of photosensitization Blum [4] mentioned two mechanisms: 1. Reactions are initiated by the absorption of light of specific wavelengths by a photo-active substance normally present whose absorption spectrum includes those wavelengths. As

3. Coblentz, W. W.; Stair, R., and Hogue, J. M.: Die spektrale Erythemreaktion der menschlichen Haut auf Ultraviolettstrahlung, Strahlentherapie **42**: 373, 1931.

4. Blum, H. F.: Photosensitization, Ann. Int. Med. **6**:877, 1933

an example of this mechanism he mentioned xeroderma pigmentosum, and assumed that the clinical characters result from a disturbance of the pigment-forming mechanism not involving the primary photochemical reaction; thus the disease should be evoked by those wavelengths which normally bring about the pigment reaction. 2. Sensitization may also be brought about by photo-active substances abnormally present; in this case the wavelength producing the reaction must lie within the absorption spectrum of the agent responsible. If one accepts this concept, eruptions evoked by wavelengths over 350 millimicrons are probably due to sensitizers; this would include the urticarial, the eczematoid and most of the vesicular eruptions. It is difficult to apply Blum's theory to an explanation of the mechanism in eruptions of hydroa.

Although experimental studies have been carried out in many cases of sensitization to light, the results have not been constant. In cases of urticaria solaris, Ward [5] and Duke [6] demonstrated sensitivity to the shorter constituents of visible light, while Beinhauer [7] could produce the lesions only with the longer ultraviolet radiations, and Frei [8] was unable to determine which of these groups was responsible.

As a rule, patients with pruriginous or eczematous reactions are found to be sensitive to visible light, but not to ultraviolet rays. Such patients have been studied by Moro, Pautrier, Payenville, Hausmann,[9] Veiel [10] and Kitagawa.[10] Urbach,[11] in a patient with prurigo aestivalis, demonstrated sensitivity to rays between 490 and 700 millimicrons. Barber and Howitt [12] observed a patient sensitive to both long ultraviolet and short visible radiations. Kreibich [13] and Haxthausen [14] found sensitivity only to ultraviolet radiations.

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5. Ward, S. B.: Erythema and Urticaria with a Condition Resembling Angioneurotic Edema, Caused Only by Exposure to the Sun's Rays, New York M. J. **81**:742, 1905.

6. Duke, W. W.: Urticaria Caused by Light, J. A. M. A. **80**:1835 (June 23) 1923.

7. Beinhauer, L. G.: Urticaria Solaris, Arch. Dermat. & Syph. **12**:62 (July) 1925.

8. Frei, W.: Lokale urtikarielle Hautreaktion auf Sonnenlicht, Arch. f. Dermat. u. Syph. **149**:124, 1925.

9. Hausmann, quoted by Arzt, L., and Hausmann, W.: Zur Kenntnis der Hydroa, Strahlentherapie **11**:444, 1920.

10. Quoted by Hausmann and Haxthausen.[1]

11. Urbach, W., and Konrad, J.: Ueber eine durch den langwelligen Anteil des Sonnenspektrums erzeugte Lichtdermatose vom Typus der Prurigo aestivalis Hutchinson, Strahlentherapie **32**:193, 1929.

12. Barber, H. W., and Howitt, F. D.: Some Observations on Light Sensitization, Guy's Hosp. Rep. **76**:314, 1926.

13. Kreibich, K.: Zur Wirkung des Sonnenlichtes auf Haut und Konjunktiva, Wien. klin. Wchnschr. **17**:673, 1904.

14. Haxthausen, quoted by Bering, F., and Barnewitz, J.: Xeroderma pigmentosum, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 4, p. 128.

Kuznitzky and Jacoby [15] carried out studies on patients with roentgen-ray dermatitis and observed increased sensitivity to ultraviolet irradiations. The immediate response to further roentgen irradiation was normal.

Gudzent [16] was unable to demonstrate sensitivity to roentgen irradiation in a case of argyria.

A review of the literature shows evidence of considerable interest in experimental studies on patients with hydroa vacciniforme. McCall Anderson was the first to observe the relationship between the excretion of hematoporphyrin and sensitivity to light, and Hausmann demonstrated experimentally that this substance could act as a sensitizer. Studies on patients with hydroa have produced rather contradictory results. Ehrmann [17] stated that his case was due to actinic irradiation; Scholtz [18] and Haxthausen [1] (two cases) found sensitivity only to visible light; Martenstein [19] found sensitivity to both visible and ultraviolet radiation in one case, while in two other cases his observations agreed with those of Möller [20] and Freund,[21] who found sensitivity to the longer ultraviolet rays, but not to visible radiations. Schmidt-LaBaume [22] recorded the unique observation of sensitivity to roentgen as well as to ultraviolet rays.

Following Ehrmann's work on disturbed porphyrin metabolism in cases of hydroa many experimental studies on porphyrin sensitization were carried out. Meyer-Betz [23] sensitized himself and observed a reaction only to visible light. Hausmann,[1] Eder,[24] Shibuja,[24] Awaki [24] and Howell [25] demonstrated that this sensitizer is most active in the field of visible light, usually involving radiations between 490 and 580 milli-

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15. Kuznitzky, W., and Jacoby, H.: Untersuchungen über die Strahlempfindlichkeit von Roentgen- und Teerhaut, Arch. f. Dermat. u. Syph. **156**:136, 1928.

16. Gudzent, quoted in Sensitization and Roentgen Rays, Editorial, Am. J. Cancer **16**:923, 1932.

17. Ehrmann: Versuche über Lichtwirkung bei Hydroa aestivalis, Sommereruption, Arch. f. Dermat. u. Syph. **77**:163, 1905.

18. Scholtz: Beitrag zur Lehre von der Hydroa aestivalis, Arch. f. Dermat. u. Syph. **85**:95, 1907.

19. Martenstein, H.: Experimentelle Untersuchungen bei Hydroa vacciniforme, Arch. f. Dermat. u. Syph. **140**:300, 1922.

20. Möller, quoted by Urbach.[12]

21. Freund, L.: Physiologische und therapeutische Studien über die Lichtwirkung auf die Haut, Wien. klin. Wchnschr. **25**:191, 1912.

22. Schmidt-LaBaume, F.: Ein besonders exzessiver Fall von Hydroa vacciniforme, Arch. f. Dermat. u. Syph. **153**:368, 1927.

23. Meyer-Betz, F.: Untersuchungen über die biologische Wirkung des Hämatoporphyrins, Arch. f. klin. Med. **112**:476, 1913.

24. Quoted by Urbach.[12]

25. Howell, quoted by Hausmann and Haxthausen.[1]

microns. Hausmann and Sonne [26] (in vitro) and Lassen [27] (in vivo) found sensitivity to the longer ultraviolet rays, an observation which corresponds more closely to the absorption curve for hematoporphyrin and related products. There is obviously considerable disagreement between observations on patients with hydroa and the results of experimental hematoporphyrin sensitization, and much can be said for or against a direct relationship between the two conditions. Some observers regard the porphyrin as the result rather than the cause of dermal sensitization to light. Not all persons with porphyrinuria are sensitive to light, nor can porphyrin and related products be found in the urine of all patients with hydroa.

REVIEW OF EXPERIMENTAL STUDIES

Gougerot [28] recognized the resemblance between xeroderma pigmentosum and roentgen-ray dermatitis, and, assumed a sensitivity to roentgen or similar radiations as a factor in its production. Löw [29] undertook the demonstration of sunlight as an etiologic agent, but used no control subjects; consequently his work was not readily accepted. Weik and Hahn [29] carried out similar studies but used different body areas on patients with xeroderma pigmentosum and controls.

Rothman [30] found no change from the normal reaction to a single period of ultraviolet irradiation, but noted a prolonged course in the disappearance of the reaction, which was followed by hyperpigmentation and telangiectasia. He found no sensitization to visible and heat rays or to moderately hard roentgen rays.

Martenstein [31] noted a delay in the development of the reactions to ultraviolet rays (a more marked reaction than in the normal subject) and delayed involution. On the changed skin, as compared with clinically normal areas, he found increased latency, less severity and more rapid recession. He found no sensitivity to visible and heat rays, but marked sensitivity to roentgen and alpha rays.

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26. Hausmann, W., and Sonne, C.: Ueber die sensibilisierende Wirkung des Hämatoporphyrins in Ultraviolett, Strahlentherapie **25**:174, 1927.

27. Lassen, H. C. A.: Ueber die Lichtsensibilisation in Ultraviolett, Strahlentherapie **27**:757, 1928.

28. Gougerot, quoted by Rost, G. A., and Keller, P., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1929, vol. 5, p. 113.

29. Löw, quoted by Rothman.[30]

30. Rothman, S.: Untersuchungen über Xeroderma pigmentosum, Arch. f. Dermat. u. Syph. **144**:440, 1923.

31. Martenstein, H.: Experimentelle Untersuchungen über Strahlenempfindlichkeit bei Xeroderma pigmentosum, Arch. f. Dermat. u. Syph. **147**:499, 1924.

Heiner [32] observed a chronicity of reaction similar to that described by Rothman and Martenstein, more marked on the unchanged than on the changed skin. Repeated ultraviolet irradiation produced no increased reaction but a definitely increased pigmentation as compared with the control. He observed no telangiectasia as contrasted with Rothman's report. His observations on other forms of irradiation agreed with those of Martenstein.

Martenstein and Bobowitsch,[33] in a second case, observed less than the normal reaction to ultraviolet radiation. The other observations corresponded to Martenstein's previous reports. There was slight sensitivity to grenz rays. The unchanged skin was sensitive to roentgen rays, but the changed skin was not. There was sensitivity to alpha but not to beta radiations.

Juon [34] observed in his case a similar latency, normal severity and chronicity with hyperpigmentation. He found this true for irradiation with both the air-cooled and the water-cooled mercury vapor arc lamp in quartz. Irradiation through a blue filter evoked a normal reaction. In a study of three cases Nakajima [35] concluded that sensitivity to ultraviolet radiation was increased in the early stages of the disease, but that later it diminished to a level lower than normal.

It may be of interest to mention the work of Usuba,[36] using intracutaneous injections of fluid from blebs produced on patients with xeroderma pigmentosum. He found the skin of persons with the incipient condition to be more sensitive than that of patients who had more extensive cutaneous changes. Inoculation of a sensitive person with the bleb serum of a normal person lowered the sensitivity of the area in which the injection was made.

In summarizing the reported studies, one notes that in four cases there was a definite sensitivity to roentgen rays. This was not demonstrated in Rothman's case. In patients tested with ultraviolet irradiation the severity of the reaction was apparently inconstant. Latency in the

32. Heiner, L.: Beiträge zur Strahlenempfindlichkeit der Haut bei Xeroderma pigmentosum, Orvosi hetil. **69**:540, 1925; abstr., Zentralbl. f. Haut- u. Geschlechtskr. **18**:217, 1925.

33. Martenstein, H., and Bobowitsch, A.: Ueber Strahlenempfindlichkeit bei Xeroderma pigmentosum, Arch. f. Dermat. u. Syph. **150**:165, 1926.

34. Juon, M.: Beitrag zu den experimentellen Untersuchungen über Strahlenempfindlichkeit bei Xeroderma pigmentosum, Arch. f. Dermat. u. Syph. **156**:367, 1928.

35. Nakajima, I.: Contributions to the Study of Xeroderma Pigmentosum, Jap. J. Dermat. & Urol. **32**:214, 1932; abstr., Zentralbl. f. Haut- u. Geschlechtskr. **42**: 216, 1932.

36. Usuba, T.: On the Photosensitizing Substance in Xeroderma Pigmentosum, Jap. J. M. Sc. Tr. **13**:139, 1932; abstr., Zentralbl. f. Haut- u. Geschlechtskr. **40**:88, 1932.

development of the erythema, hyperpigmentation and delayed involution were fairly constant findings. Martenstein and Bobowitsch demonstrated a normal reaction in their case. They tabulated the four cases reported at that time and expressed the belief that the factor of age or duration was of considerable importance. They assumed that a protective influence developed with the age of the patient and stated that sensitivity to roentgen rays reaches its peak long after the maximum sensitivity to ultraviolet radiation has disappeared.

MacCormac [37] recently presented a case in which he stated that there was no sensitivity to ultraviolet radiation. Birnbaum [38] found hyperpigmentation but no increased reaction.

EXPERIMENTS ON SENSITIVITY IN A CASE OF XERODERMA PIGMENTOSUM

I attempted to carry out detailed studies in connection with sensitivity to ultraviolet rays in the following case of xeroderma pigmentosum:

M. B., an apparently normal girl, was born Dec. 7, 1924. There was no history of consanguinity in the parents. The family history was normal as regards pigmentation and carcinoma. Seven other children were living and were apparently normal. At about 5 months of age this child was placed outdoors for long periods. Within a few days an acute erythema developed on the face, and in the course of several weeks, freckles. There was gradual progression with the usual course of the disease until I saw her in April, 1932. The child was well developed, alert and apparently normal in every other respect. The usual lesions of xeroderma pigmentosum were present on the exposed parts, including a number of keratoses and two ulcerated squamous cell carcinomas. Routine laboratory examinations gave normal results except for a white cell count of 18,000, with a slight relative lymphocytosis. The diagnosis was confirmed by biopsy. Destruction of the carcinoma by electrocoagulation was successful.

EXPERIMENTAL STUDIES

The best available method of conducting this study was by the use of radiations through light filters. Inaccuracies result from the fact that though these filters are well standardized there is no sharp cut-off at definite wavelengths. As the source of radiation, I used a high pressure, low voltage mercury vapor arc lamp with a quartz inclosure. Such a source produces a fairly continuous spectrum in the field investigated.[39]

Experiments were carried out on the trunk and thighs. As a control, identical exposures were made on the same areas of another child of about the same age and complexion.

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37. MacCormac, H.: Case Presentation, Brit. J. Dermat. & Syph. **45**:157, 1933.

38. Birnbaum: Case Presentation, Zentralbl. f. Haut- u. Geschlechtskr. **44**:140, 1933.

39. Data Submitted to Council on Physical Therapy, J. A. M. A. **99**:389 (July 30) 1932.

The following exposures were made on the two children between May 7 and July 16, 1932. Neither child received any solar radiation except the little that came through open windows.[40]

The source of light was capable of producing what we considered a standard erythema in one minute at a distance of 12 inches (30 cm.).

The first exposure of this erythema dose was made (1) through helioglass, (2) with no filter and (3) through window glass. Observations were made several times in the first twenty-four hours and each day for ten days.

1. In the patches exposed through helioglass a faint erythema was observed on each child, which appeared earlier and began to fade earlier in the child with xeroderma pigmentosum, but faded less rapidly and eventuated in hyperpigmentation. No residuum was observed on the normal child.

2. The erythema produced with no filter developed at about the same time, but that of the child with xeroderma pigmentosum never became so marked, faded less rapidly and resulted in slight scaling and hyperpigmentation. Localized deposits of pigment resembling pigmented nevi later developed in this area on the patient with xeroderma pigmentosum.

3. There was no reaction in either case to the exposure through window glass, nor did any appear following an exposure of ten minutes.

On both children an unfiltered exposure of one-half minute produced a reaction about equal to that seen after using helioglass for two minutes.

Parallel exposures were given every few days to a series of areas, using a period of one minute for irradiation through helioglass and one-half minute for exposure to unfiltered radiations. In a few of the areas larger doses were given later in the last three series of exposures. It was noticed that the patient with xeroderma pigmentosum arrived later than the normal child at the same stage of reaction. In her case the exposure through helioglass produced a more marked reaction than the unfiltered exposure; in the normal patient the reverse was observed.

Exposures of two, four and eight minutes through pyrex glass produced no reaction in either case.

Exposures of two minutes were made on three occasions through helioglass and red-purple corex glass.[41] In each patient there was a more marked reaction to exposure through corex, the reaction in the patient with xeroderma pigmentosum being greater. The exposure produced pigmentation in both, but more in the patient with xeroderma pigmentosum.

40. Figures for transmission through window glass and helio glass are based on results of tests by the United States Bureau of Standards, Washington, D. C.

41. In this and the following experiment glass filters produced by Corning Glass Works, Corning, N. Y., were used. Transmission curves are available in their booklet "Glass Color Filters."

Through helioglass the exposure which produced only a faint, rapidly fading erythema in the control was sufficient to evoke hyperpigmentation in the patient with xeroderma pigmentosum. Repeated exposures produced pigmentation in both.

Irradiation for one minute, with no filter, was applied to different areas on the body of the patient with xeroderma pigmentosum: (1) the abdomen and (2) the changed skin of the arm. The erythema was much more noticeable on the former area. Exposure for two minutes through helioglass produced a more rapid and much greater reaction than an equal exposure through clear corex.

RESULTS OF TESTS

Unfiltered Radiations.—A dose which ordinarily would produce extreme vesiculation produced only moderately erythematous and later a hyperpigmented reaction. A single dose produced a less than normal reaction, which reached its peak later and resulted in hyperpigmentation and desquamation. With repeated doses the results were similar; although hyperpigmentation appeared in both children, it was greater in the one with xeroderma pigmentosum. A much more noticeable erythema was evoked on unchanged skin than on the changed skin with a similar dose. Neither child showed a visible reaction to radiations of longer wavelengths than 350 or even 310 millimicrons in quite large doses.

With Shorter Rays.—To radiations of longer wavelengths than 280 millimicrons the reactions in both children were about equal, but hyperpigmentation developed in the child with xeroderma pigmentosum. On repeated exposure both children became pigmented, but the one with xeroderma pigmentosum more so.

When radiations with wavelengths over 250 millimicrons were used, the original erythema was greater in the normal child. Pigmentation developed in both, but became more marked in the child with xeroderma pigmentosum. This was also true of multiple exposures.

Comparison of Rays of Different Wavelengths.—In comparing the results obtained with radiations with wavelengths over 280 millimicrons and unfiltered radiations I observed that the former produced a more marked pigmentation in the child with xeroderma pigmentosum, while the normal child responded with more marked pigmentation to the unfiltered than to the filtered rays. In comparing the results obtained with rays as short as 250 millimicrons and those over 280 millimicrons, I found that the former, when transmitted by red-purple corex, produced in both children a greater reaction and more pigmentation. Radiations as short as 250 millimicrons transmitted by the clear corex did not produce as great a reaction in either child as radiations longer than

280 millimicrons. The rays transmitted through red-purple corex evoked a greater reaction than those filtered through clear corex. (The former transmits about 50 per cent more radiations from 250 to 280 millimicrons.[41])

EXPERIMENTS WITH PROTECTIVE MEASURES

Betz, while experimenting with hematoporphyrin sensitization, found that relative tolerance could be obtained by repeated exposure to the causative rays, but this tolerance was so slight and transitory as to be of no practical value. Meyer, Sellei and Liebner have protected patients with hydroa vacciniforme against exposure by the use of previous ultraviolet irradiation. Juon, in his case of xeroderma pigmentosum, observed apparent desensitization two months later on areas previously exposed to ultraviolet radiation.

Many chemicals have been suggested as a means of protection. Most of these agents act by their power of absorption of radiation. It is known that petrolatum and other bases are capable of absorbing certain radiations. Several brief and entirely qualitative experiments were conducted with irradiation of areas on the body of the patient with xeroderma pigmentosum which were covered with the following preparations (the thickness of the film was not measured): (1) petrolatum; (2) 3 per cent resorcinol in petrolatum; (3) 3 per cent tannic acid in petrolatum; (4) 3 per cent quinine sulphate in petrolatum; (5) 6 per cent quinine sulphate in petrolatum. These local applications were removed immediately following the exposure. Following an exposure, which was sufficient to produce a definite erythema on unprotected skin, there was a slight erythema with the preparation of resorcinol and none with petrolatum alone or with the other preparations. With an exposure of twice this duration there was still no erythema produced through the quinine preparations, and the erythema effected through resorcinol was more marked than that produced through petrolatum alone. I am recording these observations, but am unwilling to draw any conclusions from them. Yellow petrolatum was used in these studies.

MICROSCOPIC STUDIES

The histopathologic features of xeroderma pigmentosum are well known and have been described recently by Montgomery and Reuter.[42] They consist of:

> . . . relative and absolute hyperkeratosis; a varying degree of atrophy of the prickle cell layer, especially over the papillary bodies; irregular proliferation and prolongation of the rete ridges; intracellular edema of the cells of the epidermis,

42. Montgomery, H., and Reuter, M. J.: Xeroderma Pigmentosum: Report of a Mild Case with Histopathologic Studies, Arch. Dermat. & Syph. **26**:256 (Aug.) 1932.

with pyknosis and karyorrhexis resulting therefrom; edema of the papillary bodies and upper part of the cutis, with resultant narrowing of the rete ridges; some dilatation of the superficial vessels; a varying degree of perivascular infiltrate; a spotted melanin pigmentation of the epidermis, and, in the upper part of the cutis, chromatophores laden with pigment.

The changes in the connective tissue are not characteristic, but are also observed in senile atrophy and similar conditions. Montgomery and Reuter regard the irregular proliferation of the rete ridges in xeroderma pigmentosum as an important diagnostic feature.

Microscopic studies were made on tissue from several areas (pigmented, atrophic, keratotic and malignant). Tissue removed from an area on the forehead characterized clinically by atrophy with hyperpigmentation and depigmentation showed all the changes enumerated and no significant deviations. Examination of a keratotic lesion also gave results corresponding to those described by Montgomery and Reuter, but the proliferation of the rete was not at all marked. The carcinoma was of the squamous cell type and did not differ from those usually observed. In none of the sections were significant changes observed in the fibers of the connective tissue.

Tissue was removed following single and multiple exposures of previously normal skin to ultraviolet radiation and compared with similar sections from normal children.

Following multiple exposures to ultraviolet radiation the tissue showed all the changes enumerated except prolongation and proliferation of the rete ridges. Thus the feature which Montgomery and Reuter regard as most characteristic was absent in the pathologic changes produced artificially, although this was probably due to the short duration of the lesion rather than to any qualitative difference from the lesions usually produced by exposure to sunlight.

Following ultraviolet irradiation sufficient to produce an erythema reaction the tissue was examined and compared with tissue from a normal child showing a similar reaction. Twenty minutes following exposure no epidermal changes and no increased cellular infiltration, vasodilatation or edema could be observed.

Keller [43] described the microscopic changes present in the skin at various intervals after irradiation sufficient to produce a slight erythema. At thirty hours he observed no change in the stratum corneum or stratum granulosum; in the stratum spinosum were cells with a strongly staining cytoplasm and small nuclei encircled by a vacuole. The basal layer showed spongiositis but no degeneration, and there was a tendency to vesiculation between the cutis and epidermis. Leukocytes were observed

43. Keller, P.: Ueber die Wirkung des ultravioletten Lichtes auf die Haut: III, Strahlentherapie **16**:537, 1923.

throughout the epithelial layers as well as in and about the vessels in the cutis. Parakeratosis was not present until several days later.

Sections were made from tissue removed twenty-four hours after irradiation sufficient to produce an erythema reaction; in the skin of the normal child one could observe changes much like those described by Keller at thirty hours. There was no parakeratosis. Many cells in the stratum spinosum exhibited the homogeneity and increased staining properties described by Keller. Similar studies on the child with xeroderma pigmentosum showed, after twenty-four hours, a heavy continuous layer of parakeratosis; this feature was absent in sections from the normal child and was not found by Keller in his studies on normal persons. The nuclei of the cells of the stratum spinosum were larger and more vesicular than in the normal child or in nonirradiated skin. The change in the staining reaction of cells in the stratum spinosum which Keller regards as the most striking feature of the action of light is almost completely lacking in the child with xeroderma pigmentosum. The significance of these observations is not clear.

Becker [44] recently described changes only at the borders of the depigmented areas following irradiation of patients with vitiligo; he believed that these changes were associated with the production of pigment, since they were not seen in depigmented areas in the reaction following ultraviolet irradiation. Sections from my patient with xeroderma pigmentosum showed: (1) an irregular epidermodermal junction, (2) the presence of dendritic melanoblasts and (3) a mild cellular infiltration with some involvement of the epidermis.

SUMMARY

I have reviewed the cutaneous conditions brought about by sensitivity to light, with attention to studies which have attempted to demonstrate the radiations involved in each disease.

Urticarial reactions can apparently be evoked by either ultraviolet or visible radiation.

Patients with prurigo aestivalis have been shown to be sensitive in most instances to visible radiation.

Most workers have demonstrated sensitivity to ultraviolet rays in hydroa aestivale and vacciniforme. This is in contrast with studies on experimental hematoporphyrin sensitization in which the sensitivity may be in the field of visible light.

In xeroderma pigmentosum there is sensitivity only to radiations shorter than visible light. In most cases this includes sensitivity to roentgen rays and similar radiation. Martenstein and Bobowitsch have formulated a theory that the sensitivity to ultraviolet radiation in early

44. Becker, S. W.: Vitiligo, Arch. Dermat. & Syph. **28**:497 (Oct.) 1933.

cases later moves down the spectral scale to the shorter radiations. In spite of the somewhat similar observations on sensitivity in hydroa vacciniforme and xeroderma pigmentosum, there are essential differences in the former in the clinical picture and the presence of hematoporphyrin products. The genetic factors (predominance of males in hydroa as contrasted with an equal sex tendency in xeroderma) also may be assumed to indicate a basic difference between these conditions.

I conducted experiments on a patient with xeroderma pigmentosum, using glass filters which transmitted groups of radiations of various wavelengths.

Even on previously unexposed parts the patient with xeroderma pigmentosum, who on first exposure to sunlight in infancy responded with a marked erythema (but not vesiculation), responded with erythema and pigmentation to doses which would evoke vesiculation on normal skin.

Microscopic examination of the skin twenty-four hours after irradiation sufficient to produce erythema showed a deviation from the normal reaction. In the child with xeroderma pigmentosum changes in the cells of the stratum spinosum usually observed in normal persons were almost entirely lacking, whereas a heavy layer of parakeratosis was observed which was not seen in the normal child tested.

I could demonstrate no sensitivity to radiations of longer wavelengths than 310 millimicrons.

When exposed to radiations no shorter than 280 millimicrons the skin of the patient with xeroderma pigmentosum responded more rapidly and with more pigmentation than did the skin of the normal child.

With filtered radiations as short as 250 millimicrons the response was about normal except for the increased pigmentation.

The skin of the patient with xeroderma pigmentosum responded to unfiltered radiations less rapidly than the skin of the normal child and with more pigmentation.

The less rapid response of the skin of the patient having xeroderma pigmentosum to unfiltered radiations is probably due to a less rapid response to the shorter rays.

The reaction of the skin of the child with xeroderma pigmentosum was greater with filtered than with unfiltered radiations, while in the normal child the greater reaction followed unfiltered irradiation.

As a result of these studies the child with xeroderma pigmentosum was demonstrated to be most sensitive to radiations between 280 and 310 millimicrons. No observations were made as to the result from exposure to radiations outside the ultraviolet field.

Since few radiations shorter than 297 millimicrons reach the earth's surface it is the sensitivity to radiations of from 297 to 310 millimicrons

which is of prognostic importance to the patient, and these constitute the radiations from which the patient must be protected.

The work of Coblentz on the production of erythema by radiations of spectral distribution should be repeated on a patient with xeroderma pigmentosum as well as on patients with other types of sensitivity to light. Unfortunately equipment to carry out such a problem was not available, and I have attempted to determine the deviation from the normal reaction to irradiation in the ultraviolet field in a much less exact manner. It is apparent that similar studies must be carried out on a greater number of patients and in a more detailed and exact manner before one will be able entirely to clarify even the visible manifestations of this disease. Studies along this line must parallel biochemical and genetic studies if one is finally to understand the interesting group of diseases caused by sensitivity to radiation.

ROSACEA COMPLEX AND DEMODEX FOLLICULORUM

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In our study of the complex of rosacea we [1] were impressed with the variety of factors (especially nervous, gastro-intestinal and seborrheic) which were involved in the individual patient, and we concluded that the rational treatment of rosacea must concern itself chiefly with the constitutional indications. This concept is not new, as the studies of Ryle and Barber,[2] Lortat-Jacob and Legrain,[3] Brown,[4] Rulison,[5] Eastwood [6] and Hachenburg [7] have stressed seriatim an increasing appreciation of the variety of factors involved, especially the gastro-intestinal factors. Sellei [8] summarized this view of the situation by stating, "Rosacea exists as a result of internal causes. . . . One should never be satisfied with the external treatment alone, but should also take into account the internal treatment of the etiological factors." In contrast, the results of Ayres and Anderson [9] are startling. These authors stated that it is not "necessary to search so widely for the cause of the condition in most cases." They added that one has only to exam-

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1. Stokes, J. H., and Beerman, Herman: Effect on the Skin of Emotional and Nervous States: IV. The Rosacea Complex: A Reappraisal with Special References to the Constitutional Background and the Rationale of Treatment, Arch. Dermat. & Syph. **26**:478 (Sept.) 1932.

2. Ryle, J. A., and Barber, H. W.: Gastric Analysis in Acne Rosacea, Lancet **2**:1195 (Dec. 11) 1920.

3. Lortat-Jacob, L., and Legrain, P.: Acne Rosacea or Cuperose, Progrès méd. **38**:143, 1923.

4. Brown, W. H.: Some Observations on the Fractional Method of Gastric Analysis in Diseases of the Skin, Brit. J. Dermat. **37**:213, 1925.

5. Rulison, R. H.: Rosacea, Am. J. M. Sc. **174**:60, 1927.

6. Eastwood, S. R.: Gastric Secretion and Other Digestive Factors in Rosacea, Brit. J. Dermat. **40**:91 and 148, 1928.

7. Hachenburg, D.: Untersuchungen über Grundlagen der Rosazea, Dermat. Wchnschr. **92**:165 and 197, 1931.

8. Sellei, J.: Zur aüssern Behandlung der Rosazea, Dermat. Wchnschr. **92**: 53 (Jan. 10) 1931.

9. Ayres, S. Jr., and Anderson, N. P.: Acne Rosacea: Response to Local Treatment for Demodex Folliculorum, J. A. M. A. **100**:645 (March 4) 1933.

me a small droplet of pus obtained from a superficial pustule to find numerous Demodex folliculorum organisms, and that local antiparasitic treatment has given clinical results far surpassing anything in their experience with the disease.

Impressed by the observations of these investigators, we undertook an examination of a fresh group of cases from the constitutional and local standpoints.

REVIEW OF THE LITERATURE

A review of the vast amount of work done on Demodex folliculorum as a parasite and a possible pathogen seems essential, as apparently no report has been given in the recent American literature, even in the publication of Ayres and Anderson. Since its discovery by Berger, Henle and Simon (1841-1842) Demodex folliculorum has been an object of great study, curiosity and contention. Waves of enthusiasm in heralding Demodex as a pathogen have been stayed by the skepticism of those who insisted on the fulfilment of the laws of Koch before they accepted this organism as more than a harmless scavenger. In order to trace these trends as they relate to the problem of the interrelations between this organism and the cause of rosacea, we drew largely on the exhaustive study of Gmeiner [10] and the recent study of Fuss.[11]

Frequency of Occurrence.—The occurrence of Demodex in many different animals has been recognized by various authors as adventitious or as associated with diseased states of the skin. The parasite has been found in varying numbers in dogs, cats (rarely), pigs, cattle, goats, field-mice, rats, rabbits, bats and certain tropical wild animals. It has been found in man in varying percentages in normal and disease conditions. The percentage incidence has varied from 0 to 100 in a number of series of examinations (table 1). The cause for this variation has been the object of much study and speculation. Technical faults have a definite part in this variation, and, as has been noted in one of us (H. B.), there seems to be a periodic variation, so that on certain days the organisms cannot be found even after diligent search. Furthermore, failure to take cognizance of the variations in morphology even in the adult forms (e. g., the dwarf form of Fuss) may account for a proportion of the failures. Variation in the number of positive results of examination, however, depends on many factors other than technical ones. Chief among these are the age of the patient, the sites examined, whether

10. Gmeiner, F.: Demodex folliculorum des Menschen und der Tiere, Arch. f. Dermat. u. Syph. **92**:25, 1908. All references on Demodex folliculorum up to 1908 will be found in this article.

11. Fuss, F.: La vie parasitaire du Demodex folliculorum hominis, Ann. de dermat. et syph. **4**:1053 (Nov.) 1933.

TABLE 1.—*Incidence of Demodex Folliculorum in Normal and Disease States in Man* *

Author	Date	Total Number of Patients	Per Cent of Positive Results	Sites Studied	Comment
Studies of Normal Persons					
Simon	1842	8 dead	100	.....	Adults and children
		2 dead	0	.....	Infants
		11 living	36.4	.....	Adults and children
Henle	1845	12 dead	91.6		
Gruby	1846	60 living	66.7	Hair sac	
Wilson	1845	living	100		
Leydig	1859	living	100 (app.)†		
Geber	1884	200 living	100		
Megnin	1892	living	10	.....	Soldiers
Moniez	1896	living	10	.....	Students
Hunsche	1900	93 living	92.5	.....	Children from 6 months to 1 year of age
Guiart	1902	10 living	100		
Landois	1905	109 living	65.1		
Dubois	1910	200 living	100	.....	Persons from 20 to 85 yrs.
		living	0	.....	Persons less than 5 yrs.
		living	50	.....	Persons from 5 to 10 yrs.
		living	100	.....	Persons from 10 to 20 yrs.
Gmeiner	1908	100 dead	97	Composite body	All ages
			50	Eyelids	Second group of 100 cadavers, approximately same result
			61	Forehead	
			86	Nose	
			49	Chin	
		100 living	20-30	Face	Patients with acne punctata, vulgaris rosacea and pustulosa and comedones
Fuss	1913	100 living	100	Face	1 to 82 years
Beerman and Stokes	....	52 living	48.1	Face	15 to 69 years
Studies of Condition of the Eyelids					
Roehlmann	1899	living	25	Eyelids	Patients with trachoma
			2	Eyelids	Normal persons
Joers	1899	50 living	50	Eyelids	Normal and diseased patients
			64	Eyelids	Normal persons
			56	Eyelids	Diseased persons
Mulder	1899	living	2+	Eyelids	Normal persons
Hunsche	....	living	79	Eyelids	Normal persons
Stcherbatschoff	1903	100 living	17	Eyelids	Diseased persons
		100 dead	49	Eyelids	Normal persons
Studies of Diseases of the Breast					
Borrel et al	1909	20 dead	50	Breast	Diseased persons (carcinomas in 6 of 7)
Chambers and Somerset	1925	63 operative specimens	60	Breast	Diseased persons
Studies of Rosacea					
Gmeiner	1908	100 living	20-30	Face	Patients had acne
Kaufmann-Wolf	1925	50 living	100	Face	All women
Ayres and Anderson	1933	63 living	80	Face	
Beerman and Stokes	....	23 living	43.5	Face	Patients with rosacea
		29 living	51.7	Face	Patients without rosacea

* The references up to 1908 are from Gmeiner.
† Approximate.

the skin is dry or oily and the number of organisms in the individual follicle. External factors (drugs, etc.) as well as certain internal changes in the carrier seem to affect the organisms only slightly. General diseases of the host rarely affect Demodex; ordinarily syphilis in all of its stages, generalized gonorrhea, tuberculosis and alcoholism do not influence the organisms. Gmeiner found them in cadavers of persons who died of endocarditis, cirrhosis, pulmonary tuberculosis, pneumonia, pyelitis, carcinoma and other conditions. Fuss noted no difference in the parasites before and after a series of injections of an antigonococcic vaccine, neoarsphenamine, oleobismuth, insulin, colloidal tin, acetylcholine, tuberculin and a preparation containing sodiumcacodylate, strychnine and sodium glycerophosphate. She further observed that of three patients, one, following a series of injections of arsphenamine, had an erythrodermia and another jaundice, and in the third, after an injection of antimeningococcic serum, a violent reaction with elevated temperature and arthralgia developed; yet there was no effect on Demodex in any of the patients. In one instance thallium caused a transient disappearance of the parasites which lasted throughout the period of epilation.

Demodex folliculorum has been said to be present in persons of all ages except in new-born infants who soon after birth become infested with the parasites. Just as the actual presence of the organisms varies with age, the number varies with the subject. The number goes through a gamut: The organisms may be rare in some persons and extremely numerous in others (sixteen in a superficial scale, according to Ayres and Anderson). This variation, especially with respect to the various ages, is probably dependent on the state of the skin. In infants with smooth skin the organisms are generally rare at the pilosebaceous orifices and in places where sebaceous matter is in such small quantity as to be difficult to extract. Of the sixteen children in Fuss' series, fourteen of whom had normal skin, ten presented few of the parasites, while four harbored a large number. Of the two children who had seborrheic skins, one had few Demodex organisms and the other a large number. In summary, Fuss found that of thirty persons with normal skins, seventeen showed Demodex more or less abundantly, while in thirteen the organisms were difficult to find. In twenty-one persons with dry skin, eleven showed parasites in quantity, and ten in sparse numbers. In thirty-three persons with seborrheic skin of varying degrees Demodex was present in numbers in thirty, and rare in three persons. Fuss attempted to explain this variation in individuals as due to variations in the chemical composition and ionic reaction of the sebum.

Habitat of the Demodex.—The localization of Demodex on the topography of the skin is likewise irregular. It has been found without

an associated pathologic condition in the cerumen and the sebaceous glands of the external auditory canal, on the eyelids, nose, chin, cheeks and forehead, behind the ears, on the breasts, abdomen and back, in the nipples and on other parts of the body. The numerical distribution follows the location of the sebaceous glands. The cephalic extremity is the site of predilection. It is here that the sebaceous glands are most numerous and voluminous. However, there is no part of the skin on which the parasites can be said not to occur.

Pathogenicity.—Since its discovery there have been numerous attempts to assign pathogenic rôles to Demodex. Of the early workers up to 1874, however, Gruby was the only one to take a definite stand in this matter, according to Sparks. In 1874, Sparks saw three cases of infestation of the skin of dogs with Demodex and by analogy maintained that the organism may be troublesome to man (acne). Since 1875, various writers on ophthalmologic subjects have been divided into two camps as to the pathogenic rôle of Demodex in ocular disease. Becker, Michel, Majocchi, Burchardt, Mibelli and Stieda affirmed the pathogenic rôle of Demodex, and Stieda stated the belief that under certain circumstances it may appear on the skin without producing pathologic symptoms, while under other circumstances harmful effects are closely connected with it. By referring to table 1, one can see how variable the findings in conditions of the eye are. Roehlmann found the parasites in 25 per cent of patients with trachoma, as compared with 2 per cent of the controls. Joers, on the other hand, found them in two thirds of all normal lids. Mulder agreed with Roehlmann, but stated that the normal incidence is greater than 2 per cent. Hunsche, who found the parasites on the lids in 79 per cent of patients at autopsy, said that Demodex could cause pathologic conditions. Herzog likewise could not assign a specific pathogenic rôle to the parasite, since according to his studies micro-organisms were always associated with them. Sterbatschoff thought that the organisms are harmful in that when they are present in great numbers they open the orifice of the ciliary follicle and thereby facilitate the entrance of bacteria. In cutaneous diseases the situation is just as confused. In 1907, Lewandowsky described a patient with an impetigo-like eruption which he thought was due to Demodex canis. Babes described several patients with a cutaneous condition which he ascribed to Demodex folliculorum and which he called scabies folliculorum. De Amicis, Majocchi and Dubreuilh thought that Demodex was capable of producing pigmented cutaneous conditions. Allen reported Molluscum contagiosum due to it. Zürn saw a patient in whom the transfer of Demodex from a dog had occurred. Gmeiner failed to find Demodex in a large number of patients with alopecia,

carcinoma, eczema, furunculosis, herpes, impetigo, lichen, lupus, pemphigus, pityriasis, prurigo and trichophytosis, although he searched for the organisms microscopically. If they occurred at all, it was for the most part at the sites of sebaceous glands, and they were no more numerous there than in normal skin. Gmeiner also cited numerous writers from Simon to his own time; he found varying results in their study of acne and seborrhea. Simon, Henle, Remak, Miescher, Küchenmeister, and Zürn, Landois, Sparks, Blanchard and Fell think them causative, while the following investigators think them incapable of producing inflammation and hence lacking pathogenicity: Comby, Dubreuilh, Gaucher, Hardy, Hebra, Jarisch, Jesionek, Joseph, Kaposi, Lang, Lesser, Macleod, Mracek, Neumann, Rille, Sack, Unna, Veiel, Wolff and Ziegler.

Lawrence [12] described a form of impetigo due to the presence of Demodex, and Whitfield [13] independently described the same condition. Borrel, Gastinel and Gorescu [14] and, later, Chambers and Somerset [15] found numerous Demodex organisms in association with diseases of the breast, especially carcinoma. These investigators also were impressed with the finding of the parasites in rodent ulcers. Chambers and Somerset were unable to produce disease by inoculation into animals. Lawrence [16] found Demodex in lupus erythematosus, pityriasis alba, seborrhea and a circinate, serous, oozing condition of the beard. Weidman [17] showed specimens from a normal axilla in which Demodex was present in large numbers. He also showed slides from another case in which Demodex was found in association with hyperplasia of the sebaceous glands. Ayres [18] described a condition which he called pityriasis folliculorum and which he believed was due to Demodex. This condition was recently seen by Lawrence and Brodie.[19]

Just as the pathogenic status of Demodex is indefinite and controversial as to the conditions described earlier, so is it as to its status with reference to rosacea. In 1899, Fordyce and Holder described two

12. Lawrence, H.: On a Skin Eruption Associated with the Presence of Great Numbers of Demodex Folliculorum, M. J. Australia **2**:555 (Dec. 30) 1916.

13. Whitfield, A.: Preliminary Report, Brit. J. Dermat. **32**:312, 1920.

14. Borrel, A.; Gastinel, P., and Gorescu, C.: Acariens et cancer, Ann. Inst. Pasteur **23**:97, 1909.

15. Chambers, H., and Somerset, A. M.: Breast Disease and the Demodex Folliculorum, Lancet **1**:172 (Jan. 24) 1925.

16. Lawrence, H.: The Pathogenicity of the Demodex (Owen) in the Human Being, M. J. Australia **2**:39 (July 16) 1921.

17. Weidman, F. D.: Demodex Folliculorum in Normal Skin of Axilla, Arch. Path. **3**:904 (May) 1927.

18. Ayres, S. Jr.: Pityriasis Folliculorum (Demodex), Arch. Dermat. & Syph. **21**:19 (Jan.) 1930.

19. Lawrence, H., and Brodie, R.: Pityriasis Folliculorum (Demodex), M. J. Australia **1**:529 (May 2) 1931.

patients with rosacea in whom Demodex was found. Gmeiner was able to find the parasite in only from twenty to thirty of one hundred patients with rosacea and allied conditions. Kaufmann-Wolf [20] found it in 100 per cent of fifty cases of rosacea pustulosa in women. In 1932, Ayres and Anderson [21] cited seventeen cases in which they found Demodex in association with rosacea. In 1933, these authors had observed sixty-three cases of typical rosacea, in fifty of which Demodex was found. They regarded Demodex as an etiologic factor of importance for the following reasons:

1. The organism is easily found in from moderate to large numbers in pus from superficial lesions or in the dry follicular scales, whereas it is absent in acne vulgaris.

2. A rapid clinical improvement or cure follows the application of strong antiparasitic applications and the daily use of soap and water.

3. Accompanying the clinical improvement there is a corresponding decrease in the number of Demodex folliculorum organisms that can be isolated from the skin.

Our results have not shown that Demodex is more prevalent in patients with rosacea than in others. It was present in 43.5 per cent of patients with rosacea, as compared with 51.7 per cent of normal persons, and if Demodex is pathogenic we may attribute this property to the following facts:

1. By their sole presence in large numbers in the follicles, they may when mixed with sebum form a foreign body which may not only modify the normal aspect of the follicles and glands but also excite and irritate the cells of the germinative layer of the sebaceous glands; the sebaceous glands then react by hypersecretion, which besides favoring seborrhea may pave the way for secondary infection (Fuss).

2. In cases of rosacea in which Demodex occurs in large numbers (this is rare in our experience) the reflex vasomotor flushings of the skin probably make the soil suitable for the growth of the parasite, especially if the patient is subject to a keratotic condition of the skin in the region of the rosacea. Lawrence stated, "In some of these cases . . . the Demodex undoubtedly produces a good deal of inflammation, favoring secondary pyogenic infection."

3. Demodex may favor the entrance of more or less virulent bacteria or viruses into the hair follicles; that is, it may open the gate by mechanical action (Herzog, Brons, Borrel and Dubois [22]).

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20. Kaufmann-Wolf, M.: Concerning the Usual Presence of Demodex Folliculorum in the Pustules of Acne Rosacea, Dermat. Wchnschr. **81**:1095 (Jan. 25) 1925.

21. Ayres, S. Jr., and Anderson, N. P.: Demodex Folliculorum: Its Rôle in the Etiology of Acne Rosacea, Arch. Dermat. & Syph. **25**:89 (Jan.) 1932.

22. Dubois: Recherche du Demodex folliculorum hominis dane la peau saine, Ann. de dermat. et syph. **1**:188 (April) 1910.

MATERIAL

Our material consisted of fifty-two patients from the clinic. Twenty-three had rosacea in varying degrees of severity, and the remaining twenty-nine had normal skin or various dermatoses involving the face. Fourteen were normal; six had acne vulgaris; two, seborrhea; one, dermatitis; two, lupus erythematosus; two, sycosis of the beard, and two, erythema multiforme.

CLINICAL SUMMARY

Constitutional Background of Rosacea.—In our original study we found that the following factors ranked as major influences: the seborrheic habitus (80 per cent), nervous factors (76 per cent) and gastro-intestinal disturbances (66 per cent). In our present series of twenty-three patients the seborrheic habitus was present in 83 per cent, the nervous factors in 65.2 per cent and the gastro-intestinal disturbances in 48 per cent. In this series focal infection, while numerically less important than in our first series (22 per cent in this series as compared with 51.9 per cent in our first series), was apparently responsible for a flare-up in at least five patients, and a menstrual flare-up of rosacea was noted in three of the ten female patients. This series of patients collected from the clinic in contrast with our original series collected from the private practice of one of us (J. H. S.) contained more men than women. This is in direct agreement with the suggestion of Low [23] that, relatively speaking, men are more likely to seek advice in clinics, and women more likely to seek it in private practice. Hence, in summary, the constitutional factors in the present series correspond closely with those of our original series.

Demodex Folliculorum in Patients with Rosacea and in Controls.—The technic of Ayres and Anderson in the search for Demodex in patients with rosacea and in the controls was carried out in detail. Droplets of pus, numerous comedones and superficial scrapings from the area of rosacea were placed in a 20 to 40 per cent potassium hydroxide solution and examined under the microscope with the low and high power objectives. Whenever negative results were obtained, repeated searches were made on the same day or on successive days. We felt that this was necessary because one of us (H. B.), who usually presents numerous Demodex organisms and trichostasis spinulosa in the nasal follicles, noted in a series of examinations carried out over nine months that there were certain days when in spite of repeated searches no Demodex or trichostasis could be detected. It is interesting to note that in confirmation

23. Low, Cranston: The Association of Eye Lesions with Rosacea, Brit. J. Dermat. **34**:275, 1922.

of Williams'[24] and Fanburg's[25] contention trichostasis was present in a fair percentage of the group examined.

The results of our search are given in table 2.

Ayres and Anderson noted that their patients used soap infrequently, and they felt that the excessive use of cold cream and powder and the substitution of cleansing cream for soap and water favor the development and multiplication of the organisms. In striking contrast, forty-six of our fifty-two patients used soap and water from one to four times a day; one did not use soap, and in five patients there were no data. The patient who did not use soap showed no Demodex. Of the forty-six patients who used soap, twenty-five manifested Demodex, and twenty-one did not. Incidentally, the soap used by the largest number of patients (eight) was a highly advertised antiseptic soap.

Our data are meager with regard to cold creams. Of the ten patients who used considerable cream, eight showed Demodex, suggesting that the use of cream favors the multiplication and development of Demodex.

TABLE 2.—*Results of Search for Demodex Folliculorum*

Group	Number of Cases with Positive Results*	Number of Cases with Negative Results	Per Cent of Cases with Positive Results
Entire group (patients with rosacea and controls)	25	27	48.1
Controls (normal persons and patients with other dermatoses)	15	14	51.7
Patients with rosacea	10	13	43.5

* The results were considered to be positive if the organisms were found in any of the sites studied.

Therapeutic Effect of Sulphur in Rosacea.—The comparative evaluation of sulphur as a therapeutic agent in the treatment of rosacea is difficult because in the constitutional management of the condition we have previously employed this drug in mild concentration mainly to combat the seborrheic factor. Ayres and Anderson stated that the improvement which they noted after the use of strong applications of sulphur was not due to the effect of the sulphur on the seborrhea, because some of the most striking results occur in cases presenting dry skins with no evidence whatever of seborrhea. The toxic action of various agents on Demodex folliculorum separated from the body is very different from that which occurs when the reagents are applied to the skin in man. Gmeiner found that parasites isolated from the follicles were rapidly destroyed by antiscabetic ointments, especially the naphthol ointment of Kaposi,[25a] which killed them in one and one-quarter

24. Williams, C. M., in discussion on Burgess, J. F.: Trichostasis Spinulosa, Arch. Dermat. & Syph. **25**:40 (Jan.) 1932.

25. Fanburg, S. J.: Trichostasis Spinulosa, Arch. Dermat. & Syph. **27**:274 (Feb.) 1933.

25a. Kaposi's naphthol ointment is composed of: naphthol, 15 Gm.; soft soap, 50 Gm.; powdered white chalk, 10 Gm., and lard, 100 Gm.

minutes; Jarrish's modification of the Kaposi ointment [25b] and the Wilkinson-Hebra salve [25c] destroyed the organisms in from four to five minutes. This conception of the rapid destruction of Demodex by sulphur under living conditions on the human body does not seem acceptable on several grounds. Except in one instance, we were unable to verify the conception of the surface prevalence of the parasite as emphasized by Ayres and Anderson. In several instances, a week after the use of antiscabetic ointment, we were actually able to obtain living Demodex in scrapings when a previous examination had given negative results. Our stand is further substantiated by the recent and detailed studies of Fuss. This author, while able to find Demodex in 100 per cent of her cases, stated that she was rarely able to obtain specimens from the surface of the skin. In the few instances in which this result was obtained she considered that the organisms were on the surface merely as a result of overflow, since the follicles in the patients were loaded with Demodex. Fuss stated further that external conditions only slightly affected the parasites "deep in their lair." The most meticulous hygienic care, the most frequent soapings and creams, "paints" and powders do not influence the development of the parasites. Washings with alcohol or ether and applications of tincture of iodine over a prolonged period are also without effect on them, although experimentally, outside the body, alcohol kills the organisms in three minutes, tincture of iodine in two minutes and ether instantly. Sulphur ointments and other topical applications are no more effective. Furthermore, Sabouraud [26] considered that there is no better established dermatologic certainty than that it is impossible to free an affected person by external applications. He stated that when the parasites introduce themselves into the follicles parasiticides do not touch them.

Irrespective of the theoretical basis for the use of sulphur in rosacea, we agree with Ayres and Anderson that so far as the local management of the patient is concerned sulphur plays an important part in the involution of the individual attack. Some patients with rosacea cannot tolerate even low percentages of sulphur, while others in our present series have used 10 per cent sulphur ointment daily for several months.

To test the therapeutic efficacy of this agent in rosacea, our constitutional regimen was replaced wherever possible with the local use of 10 per cent sulphur alone or as the antiscabetic ointment with 10 per cent balsam of Peru. In some instances after a fair trial and in response

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25b. Jarrish's modification of Kaposi's ointment is composed of: naphthol, 10 Gm.; flowers of sulphur, 10 Gm.; lard, 100 Gm.; soft soap, 50 Gm., and white chalk, 10 Gm.

25c. Wilkinson-Hebra's salve is composed of: flowers of sulphur, 40 Gm.; oil of cade, 40 cc.; soft soap, 80 Gm.; powdered white chalk, 5 Gm., and lard, 80 Gm.

26. Sabouraud, R. (J. A.): Entretiens dermatologiques à l'ecole Lailler (Hôpital Saint-Louis), Paris, Octave Doin et fils, 1913, p. 40.

to the patient's demands we were forced to resort to our constitutional regimen. Our results with the local treatment are given in table 3.

A comparison of these results with those of our previous series is given in table 4.

TABLE 3.—*Results with Local Treatment in Sixteen Patients*

Degree of Improvement	Number Improved	Demodex Present	Demodex Absent
Greatly	2	1	1
Average	7	3	4
No improvement	7	2	5

TABLE 4.—*Comparison of Group Treated with Sulphur and Group Treated Constitutionally*

	Grade of Improvement (Scale 1-2-3-4)		
	None	1 to 2	3 to 4
Group treated with sulphur	7 (43.75%)	7 (43.75%)	2 (12.5%)
Group treated constitutionally	6 (9.1%)	26 (39.4%)	34 (51.5%)

Briefly stated, we obtained good results (grade 1-4) in 56 per cent of the series of patients treated with sulphur as compared with 91 per cent of good results in the patients treated locally and constitutionally. This suggests that in spite of the worth of sulphur alone, used locally, the combined attack has a significant advantage.

SUMMARY

1. A new series of twenty-three patients with rosacea has been studied from the standpoint of constitutional and local parasitic factors. The same constitutional factors (seborrheic, gastro-intestinal and nervous) were present in about the same frequency as in the series reported by Stokes and Beerman. Demodex folliculorum was not present in more patients with rosacea than in the controls (43.5 in the former as compared with 51.7 per cent in the latter) or in greater numbers than in twenty-nine other patients, including fourteen normal persons.

2. A survey of the literature on Demodex folliculorum shows that the controversy with reference to its pathogenicity is old. The weight of evidence is against its causing any condition. Likewise, no conclusive etiologic rôle can be assigned it in rosacea. It is possible, however, that by a numerical increase it may act as a vector of virulent organisms into the follicle or mechanically open the gateway for the entrance of these bacteria or viruses, or it may reflexly increase the flushing of the area of rosacea and predispose to a secondary invasion.

3. Sulphur locally is of value in the treatment of rosacea, but when it is combined with constitutional management based on factorial analysis, the effectiveness of treatment is almost doubled (91 per cent of good results with sulphur and constitutional treatment as compared with 56 per cent of good results with sulphur alone).

PEMPHIGUS

EFFECT OF PEMPHIGUS SERUM ON THE LEUKOCYTIC PICTURE OF RABBITS

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As there appears to be evidence of the presence of a toxic substance in the blood serum in pemphigus,[1] it is reasonable to assume that this substance is present in relatively large quantities in the blood stream in the last few hours preceding death due to this disease.

In this paper an attempt has been made to demonstrate the presence of this toxic substance by determining the effect of intravenous injection of pemphigus serum on the white cell count of rabbits.

The material used for the study was blood serum taken from two fatal cases of pemphigus within twenty hours preceding death. The histories of the cases, together with certain studies of the blood and bacteriology made thereon, have already been reported.

METHOD

In the carrying out of this work it was necessary to establish a normal base line for the rabbits' differential white cell count before the injection of the pemphigus serum. This was done by performing five differential counts daily at the same hours on three successive days, with a fixed time, quality and quantity of feeding. The animals were fed at 8 a. m., and bleedings were made at 9:30 a. m., 10:30 a. m., 11:30 a. m., 12:30 p. m. and 2:30 p. m. The serum in quantities of from 1 to 3 cc. was injected into the marginal ear vein of the rabbit, and blood for differential counts was taken at the same hours as before the injection of the serum. Counts were continued for three days after injection, and feeding details were unaltered.

A similar series of differential counts was made with another set of rabbits in which from 1 to 3 cc. of normal human serum was used.

EXPERIMENTAL RESULTS

Three rabbits were used for each serum, and the results obtained were in close agreement with one another. None of the animals except one showed any untoward effects from the injection of the serum, and

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1. Pels, I. R., and Macht, D. I.: Phytopharmacologic Examinations of the Blood in Pemphigus, Arch. Dermat. & Syph. **19**:640 (April) 1929; Phytopharmacology of Pemphigus, ibid. **23**:601 (April) 1931.

all were alive and well four months after the injection. The affected animal received 3 cc. of normal human serum and collapsed at once. The lymphocyte count rose considerably, and the pseudo-eosinophil count was depressed but rose rapidly after five hours and was above 60 per cent when the last count was made, twenty-eight hours after injection. The animal died during the same night.

Blood smears were stained with Wright's stain, and not less than 100 cells were counted.

At the beginning of the work differentiation between the pseudo-eosinophils and eosinophils of the rabbits' blood caused a little difficulty, which was soon overcome with practice. The pseudo-eosinophils are really polymorphonuclear leukocytes and were well described by Scarborough,[2] who wrote:

> These cells are about 10 to 12μ in diameter. The nucleus is polymorphous, most often bi- or tri-lobed. The granules are numerous but not as densely packed as are eosinophilic granules. They are larger than the neutrophilic granules of man, but slightly smaller than the human eosinophilic granules. They are ⅓ to ¼ the size of the eosinophilic granules. Ability in differentiating these cells from the eosinophils is acquired by experience, and identity is established chiefly by the size of the granules.

The results of this work show that there is no significant difference between normal serum and that from advanced cases of pemphigus in the effect on the differential white blood cell count of the rabbit. The differential white cell count of the rabbits used was, before injection, approximately:

	Per Cent
Lymphocytes	60
Large monocytes and transitionals	10
Eosinophils	2
Basophils	3
Pseudo-eosinophils	25

Following injection of the normal and pathologic serums there was a rise within three hours in the pseudo-eosinophil proportion to approximately 40 per cent and a diminution in the lymphocyte proportion to 40 per cent, the proportions of the other elements of the white cell picture remaining unchanged. The fact that the leukocytes of the rabbit give the same reaction to normal human serum as to serums from advanced cases of pemphigus indicates that this method cannot be used to demonstrate the presence of a toxic substance in the blood in cases of pemphigus.

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2. Scarborough, A.: The Blood Picture of Normal Laboratory Animals, Yale J. Biol. & Med. **3**:80 (Oct.) 1930.

DISORDERS OF THE FEET AS A CAUSE OF RESISTANT ECZEMATOID RINGWORM

THEIR INFLUENCE ON THE AMOUNT OF SWEATING OF THE FEET

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For some time I have been struck with the observation that some patients with resistant cases of eczematoid ringworm infection also have orthopedic disorders of the feet or wear imperfectly fitting shoes. In several cases, correction of these difficulties resulted in a speedy eradication of a previously resistant dermatitis and relief from hyperhidrosis, or both. Many investigators have felt that the disposition toward ringworm infection has some connection with excessive perspiration. My own experiments, previously reported in a series on the self-sterilization powers of the skin, seem to substantiate this view.

To obtain quantitative facts for my empirical observations, I took the patients to the laboratory. Two objectives were sought: (1) to ascertain the amount of sweat secreted by the sole before and after correction of flatfootedness (pes planus) and (2) to produce mild discomfort of the foot by shortening the shoe and observing the effect on the amount of sweat secreted.

METHOD

A layer of absorbent cotton was placed between layers of gauze and shaped as a last for the shoe of the person tested. When the shoe was to be shortened to produce cramped quarters, a similar pad was inserted into the toe of the shoe. Usually one side was shortened and the other not, the latter thus acting as a control. The materials were weighed before and after the patient had used them in his shoes and had walked about for two hours. The difference between the weights before and after the test was taken as representing the amount of sweat secreted.

RESULTS

Six cases of hyperhidrosis were observed before and after correction of improperly fitting shoes or flatfootedness. Three patients had eczematoid ringworm; one acute and the other two chronic. The other three patients had only intertriginous scaling. The weight in milligrams for the latter three before correction was 854, 1145 and 778 and after correction, 175, 288 and 526, respectively. The weight for the acute

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case was 1,865 before, and 170 after, correction. (The figures for the weight before correction were undoubtedly swelled by secretions other than sweat.) In two cases of chronic hyperhidrosis the figures were 642 and 763 before, and 394 and 258 after correction.

Thirty-one persons who had their shoes shortened as described were studied. The first figure in each case was for the shortened side, and the second for the control or nonshortened side. These fifteen sets of figures are representative of the rest.

1. 448-221	6. 279-156	11. 363- 144
2. 506- 30	7. 726-697	12. 981-1,012
3. 181- 2	8. 31- 64	13. 517- 226
4. 1,290-612	9. 184-151	14. 115- 192
5. 349-330	10. 72- 60	15. 78- 27

In nos. 5, 7 and 12 there were no increases on the shortened sides. These were cases of decided flatfootedness in which the feet were probably secreting as much sweat as they were capable of even without shortening. When the additional stimulus of making the foot uncomfortable was added, the feet were incapable of responding to it by further secretion.

Two interpretations come to mind to explain the hyperhidrosis associated with flat feet. The first is that the condition gives rise rapidly to fatigue of the extremities in walking, and fatigue, like asthenia, increases sweating. The other explanation is that a flatfoot lengthens when one stands on it. It may be perfectly comfortable when the shoe is put on, but, because the foot lengthens only as it is being used, mild discomfort comes on too slowly to be easily appreciated. Nevertheless, there is sufficient discomfort to stimulate secretion of sweat. (It is known that pain may do this.)

Aside from the fact that flatfootedness was the obvious cause of hyperhidrosis and perhaps of ringworm infections in some of the patients, the single factor that impressed me most often was the frequency of shoes that were too short. Moreover, the short shoes were apparently not exciting conscious discomfort, yet practically all the patients who agreed to wear shoes that fitted better, and did wear them, confessed to increased comfort. Certainly, either the resistant tineal infections or the hyperhidrosis was improved.

It seems that the factor of relative humidity should have been accounted for in evaluating these results. Although this relationship was not lost sight of, in one set of figures it had no bearing. For instance, in the experiments in which the shoe was shortened on one side, the other side acted as the control, so that no matter what the relative humidity was there was a perfect control for each test. In the other

experiments, the finding before and after correction of shoes was uniformly decreased sweating, the relative humidity making no decisive difference.

SUMMARY

1. Orthopedic conditions of the feet, such as flatfootedness and shoes that are too short may be one cause of the resistance of eczematoid ringworm infection to treatment.

2. A resistant infection of this sort sometimes responds promptly to routine therapy after proper orthopedic corrections are made or after well fitting shoes are worn.

3. The amount of sweat secreted by such feet is decidedly decreased when deformities are corrected or when shoes are properly fitted.

4. The wearing of shoes that are too short increases sweating of the feet.

RINGWORM OF THE SCALP

A REPORT OF THREE CASES DUE TO MICROSPORON LANOSUM WITH A TENDENCY TO SPONTANEOUS RECOVERY

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Sabouraud [1] described instances of spontaneous cure in patients with ringworm of the scalp and also recognized that this tendency was limited almost entirely to cases in which the causal organism was also pathogenic to certain of the lower animals. Since infections of the scalp due to Trichophyton are rarely seen in New York, the main excitants in that group are the so-called animal microsporons, of which Microsporon lanosum is the commonest. When tinea capitis is due to M. lanosum, the symptoms may be clinically similar to cases in which Microsporon Audouini and related organisms are responsible by showing patchy involvement and exhibiting very little inflammatory reaction in the involved areas. At other times the patches are erythematous, and follicular pustules may be present. Kerion formation may be noted. When present in untreated patients, the latter symptoms are suggestive of "animal" infection.

Examination of infected hairs in a potassium hydroxide preparation reveals the presence of fungous material, but it is difficult, if not impossible, to differentiate in this way between the various types of microsporons. It would thus be advantageous, since the choice of treatment might be influenced, to make cultural as well as microscopic studies as a routine in the management of all ringworm infections of the scalp. The three following cases illustrate a tendency to biologic cure in which drastic therapeutic measures were unnecessary.

REPORT OF CASES

CASE 1.—J. W., a girl, aged 10, when examined on Jan. 26, 1932, stated that an involvement of the scalp had been present for two months. An eruption was noticed on her body a week before examination. No treatment had been given. Her sister, R. W., aged 4, had an erythematous ringed lesion on the right side of the neck of two weeks' duration.

There was loss of hair in scattered areas on the scalp, all of which were erythematous and scaly. Scaliness was noted particularly at the periphery of the

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1. Sabouraud, R.: Les teignes, Paris, Masson et Cie, 1910, p. 214.

lesions. A carbuncle-like lesion, 4 cm. in diameter, was present over the vertex, with a few swollen, pustular lesions on other areas of the scalp. The posterior auricular and cervical glands were enlarged. There was also a follicular eruption on the trunk, consisting of small erythematous papules.

No fluorescence of the hair of the scalp was present when examined under the Wood filter. Repeated extemporaneous and cultural studies of the hair and pus were entirely negative. However, scrapings from the lesion of the neck of the sister revealed sporulated mycelia, and on culture a typical colony of M. lanosum developed. Hanging-drop cultures confirmed this observation. Trichophytin in patch tests (in dilutions of 1 : 10 and 1 : 30) were strongly positive in both children. In view of the negative mycologic findings, epilation was not considered. Instructions were given to wash the scalp daily, and an ointment containing 6 per cent of ammoniated mercury was prescribed. On March 12, 1932, the kerion had disappeared, and in its place was an atrophic, depressed scar; it was believed that in this area permanent alopecia would result. Hair was returning to all the other areas.

CASE 2.—F. C., a boy, aged 6, when first seen on Nov. 26, 1932, gave a history of ringworm of the scalp of two months' duration. The disease was treated in another clinic one month previously; partial epilation of the hair of the scalp had taken place following a single roentgen treatment. No history of contagion was obtained.

On examination, a fairly diffuse alopecia of the scalp was noted, interspersed with tufts and scattered hairs which had apparently resisted the depilating dose of roentgen rays which had been administered. In addition, there were scattered, erythematous lesions in which follicular pustules were situated. Crusts and scales were also present. There was an enlargement of lymph nodes in the posterior auricular and cervical regions. A papular, scaly, follicular eruption was noted over the back and on the right arm. Fluorescence of a greenish hue was visible in scattered points over the scalp when it was observed under the Wood light.

Examination of the hair in a 15 per cent solution of potash revealed sheets of spores. Colonies of M. lanosum developed on cultures, and the observation was confirmed in hanging-drop cultures.

Since it was not considered desirable to use further roentgen therapy at the time, and in view of the inflammatory character of the disease, topical treatment was instituted. An ointment containing 3 per cent of ammoniated mercury was first prescribed. This was later increased in strength to 10 per cent. Clinical improvement was noted after several weeks, but fungi could still be demonstrated. A salve containing 2 per cent oil of cinnamon, 2 per cent thymol and 2 per cent iodine crystals was then applied daily. No irritation developed, and the disease gradually disappeared. On May 27, 1933 (six months after the first admission), there was a clinical cure; no fluorescence was present under the Wood light, and no hairs suitable for examination could be found. On July 15, 1933, since all evidence of the disease was absent and total regrowth of hair had taken place, the patient was discharged.

CASE 3.—C. D., a well nourished girl, aged 7, was admitted to the clinic for diseases of the skin on March 14, 1933. Six weeks before admission, an area of acute inflammation was noticed on the scalp, resulting in loss of hair. Other lesions rapidly developed, all being localized, inflamed and slightly tender to the touch. An ointment containing 6 per cent of ammoniated mercury had been applied once a day for two weeks. The father stated that several other children in the neighborhood had similar infections of the scalp. A dog belonging to the family had falling hair and scaly patches on the body.

An examination disclosed many small erythematous lesions devoid of hair in the left parietal region and several similar lesions on other parts of the scalp. In some areas pustulation and formation of crusts were noted; in others the active process had resolved, leaving depressions which appeared to be atrophic.

No short stumps were found for examination, and longer hairs examined were normal. Clumps of spores were found in pus, and on culture the organism was determined to be M. lanosum. Hanging-drop culture revealed numerous fuseaux. A Wassermann test was negative. A trichophytin patch test was strongly positive. No fluorescence of hairs was observed when the scalp was examined under the Wood light.

Since the patient was one of seven children in a poor family, it was considered best to institute treatment in spite of the obvious near cure. Instructions for hygienic care were given; the scalp was washed twice a day and an ointment containing 3 per cent ammoniated mercury was applied morning and night. A month later no pustulation or crusting could be detected. In two months a considerable regrowth of hair had occurred, and no erythema was visible. In one area in the left parietal region (1 cm. in diameter), the scalp was depressed and atrophic, indicating that permanent alopecia was probable.

SUMMARY AND COMMENT

In three patients with tinea capitis, positive diagnoses of infections due to M. lanosum were made in two instances. In case 1 the same organism was isolated from a lesion of tinea circinata in a sister, suggesting that it was responsible for the infection on the scalp.

In all patients the clinical symptoms included well defined patches of alopecia, which showed a marked inflammatory reaction, including erythema, scaling, pustulation and crusting. The final result in all was excellent, with the exception of a small area of permanent atrophy and alopecia in cases 1 and 3. In those two patients the infection was entirely cured within three and a half months of its inception; in the other patient the disease was present for eight months. It was considered that treatment played a minor rôle in the recovery of two patients (cases 1 and 3); the therapeutic measures employed in the other patient probably hastened the cure. This indicated that some infections due to M. lanosum are amenable to topical therapy. The well known resistance to cure by local treatment in "gray-patch" ringworm points to an important biologic factor rarely seen when organisms of the M. Audouini group are the excitants.[2] For this reason cultural studies are believed to be of importance in the management of ringworm of the scalp. When this is impossible, it is suggested that some cases in which an inflammatory reaction is present may require neither depilating measures nor intensive topical treatment in order to effect a cure.

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2. Cases are not unknown in which acute inflammation and even kerion formation follow infections due to M. audouini (Fox, H.: Ringworm of the Scalp in the Adult, Arch. Dermat. & Syph. **13**:398 [March] 1926).

MULTIPLE BENIGN TUMOR-LIKE NEW GROWTHS OF THE SKIN

REPORT OF A CASE

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In 1891, Schweninger and Buzzi [1] published their report of "Multiple Benign Tumor-Like New Growths of the Skin." Briefly, according to the authors' description, the condition is characterized by the appearance of numerous white to slate-colored, bladder-like lesions beneath the skin, some of which have fine telangiectases coursing over them. The eruption involves the upper part of the back, chest, shoulders and arms. The lesions vary in size from that of a lentil to that of a sixpence and on the sides of the thorax are arranged along the lines of cleavage. By pressure with the tip of the finger, most of the formations can be forced into the deeper skin, producing a shallow pit on the surface, the tumor reappearing, however, like a ventral hernia when the pressure is released. The disease is slowly progressive, new lesions occurring as the older ones involute spontaneously, leaving soft, flat scars.

Histologically, there are an absence of elastic tissue in the central portions of the lesions and an increased quantity peripherally. Accumulations of small round cells are seen about the superficial horizontal capillary network and the vessels of the glandular structures. The sebaceous glands are frequently enlarged. The epidermis is thinner over the affected parts.

For many years following the classic description of Schweninger and Buzzi there were no reports of the disease in the literature. In 1917, Pusey [2] described the second reported case and reawakened interest in this strange malady. Since that time, twenty-four cases of multiple benign tumor-like new growths of the skin have been reported in the literature or presented at society meetings. Combes [3] and more recently Chargin and Silver [4] thoroughly reviewed the literature on these tumors and discussed their relation to macular atrophy in general.

From the Department of Dermatology and Syphilology, Reading Hospital.

1. Schweninger and Buzzi: Multiple Benign Tumor-Like New Growths of the Skin, Internationaler Atlas von seltener Hautkrankheiten, Leipzig, Leopold Voss, 1891, plate 15.

2. Pusey, W. A.: A Case of Multiple Benign Tumor-Like New Growths of Schweninger and Buzzi, J. Cutan. Dis. **35**:582, 1917.

3. Combes, F. C., Jr.: Idiopathic Macular Atrophy, Arch. Dermat. & Syph. **22**:1022 (Dec.) 1930.

4. Chargin, L., and Silver, H.: Macular Atrophy, Arch. Dermat. & Syph. **24**: 614 (Oct.) 1931.

REPORT OF CASE

History.—D. H., a white girl, aged 11 years, was referred to the dermatologic clinic because of a cutaneous condition that had begun five years previously, at the age of 6. The eruption caused no discomfort except a slight itching when the patient was "overheated." Appearing first on the shoulders and the upper part of the chest, the eruption spread to the neck and extensor surfaces of the arms and forearms. One lesion occurred on the forehead and another on the cheek. There was no history of an antecedent eruption of any kind, and as far as could be ascertained, the process had always been clinically noninflammatory.

The general health of the patient was good. The menses had not yet begun. As an infant, she had suffered from rickets; in early childhood, she had scarlet fever and whooping cough.

The family history was interesting for reasons to be discussed later. Through three generations on both sides of the family there was a history of immorality, alcoholism and mental deficiency. The child's mother had syphilis of many years' standing, and in a previous marriage had given birth to a feeble-minded son. The father was chronically alcoholic, and had been classified by one psychiatrist as a middle-grade moron and by another as a constitutionally inferior person of the inadequate type. From this union there were eight pregnancies, which included a macerated fetus, a high grade moron son, a low grade moron daughter, our patient, who developed macular atrophy and was of a borderline mentality, a miscarriage, a daughter who died in infancy and two daughters of normal mental ability. All the children had difficulty in learning to speak. Of the five living children, we have been able to trace four, none of whom present clinical or serologic evidence of syphilis. In addition to the immediate family, there were several mentally defective uncles and cousins on the paternal side.

Physical Examination.—The patient was a short, stocky, restless child. The height was 53 inches (134.6 cm.), and the weight 80 pounds (36.3 Kg.). Although rather heavy for her height, she presented no evidence of endocrine imbalance. The gait, station and tendon reflexes were normal.

The temperature ranged persistently from 99 to 100.1 F., the higher temperatures being recorded in the afternoon. The pulse varied between 90 and 100, with 20 respirations per minute. The blood pressure was 116 systolic and 76 diastolic.

The general physical examination failed to reveal any pathologic changes of the heart, lungs or abdomen. A search for stigmas of congenital syphilis was likewise fruitless. The ophthalmologic examination revealed compound hyperopic astigmatism. Left ethmoid sinusitis was reported by the laryngeal consultant. A slight vaginal discharge was present.

Examination of the Skin.—There were two types of cutaneous lesions present. The more recent lesions, as those on the arms and forearms, were round or oval, soft, circumscribed, bladder-like, bulging elevations varying in color from that of the skin to a slate tint. They ranged in size from 2 or 3 mm. to 2 cm. These herniated lesions disappeared when the skin was stretched. On light palpation, in regions where the skin was freely movable, the swellings could be made to disappear, the impinging finger slipping into a hollow and sensing a firm resistance to lateral pressure about the periphery of the lesion. On withdrawing the pressure, the swelling would promptly recur. The skin over the swellings appeared normal in texture, and lanugo hairs were present. Fine telangiectases were seen coursing over many of the tumors.

Over the shoulders, neck and the upper part of the chest (fig. 1), there was an older type of lesion. The soft, tumor-like growths had involuted and been replaced by flat, grayish, shriveled, atrophic macules. In these regions, a tendency toward grouping was observed. On the sides of the neck, the oval atrophic lesions were arranged with their long axes along the lines of cleavage. In a few instances, the scars were slightly depressed below the level of the surrounding skin. When relaxed, the skin of the atrophic macules became folded as if there were an excess of skin present. There were about two hundred lesions in all.

Laboratory Studies.—Laboratory and clinical tests failed to reveal a possible etiologic factor in this case. The urine was normal in all respects. The blood sugar and urea nitrogen were 102 and 12 mg. per hundred cubic centimeters, respectively. There were 10.5 mg. of calcium and 4.2 mg. of phosphorus. The

Fig. 1.—Typical herniated lesions and atrophic macules. The photograph was taken with the shoulders drawn back, producing wrinkling of the atrophic macules as if an excess of skin were present.

blood count revealed 4,050,000 red cells per cubic millimeter, with 70 per cent hemoglobin and slight anisocytosis. There were 5,000 white cells, of which 50 per cent were polymorphonuclears, 3 per cent eosinophils, 44 per cent lymphocytes and 3 per cent mononuclears. Repeated blood Wassermann and Kahn tests were uniformly negative. The provocative Wassermann and Kahn series, following an injection of 0.3 Gm. of neoarsphenamine, were likewise negative. Examination of the spinal fluid showed: Wassermann test, negative; colloidal gold curve, 0000000000; globulin, normal; the cells, 4. The roentgen examination of the chest gave no evidence of tuberculosis or other pathologic condition. The clavicles and tibias revealed no periosteal thickening on roentgen examination. Mantoux tests performed with dosages of 0.01, 0.1 and 1.0 mg. of old tuberculin gave no reaction. Repeated blood cultures showed no growth.

Histologic Examination (Dr. Fred D. Weidman).—The epiderm was definitely thinner than normal, consisting of four or five layers of cells on the

average. The stratum corneum was represented by only a few shreds of keratotic substance. Interpapillary pegs were scarcely recognizable; they were indicated by a few short projections distributed at wide intervals. The epiderm was of uniform thinness throughout the entire section. The fibrillae were of extreme delicacy but at the same time did not give any indication of edema. The hair follicles were also delicate in construction; the sebaceous glands in particular were hypoplastic. There were no important infiltrations of round cells around the blood vessels, although there was a moderate grade of swelling of their lining

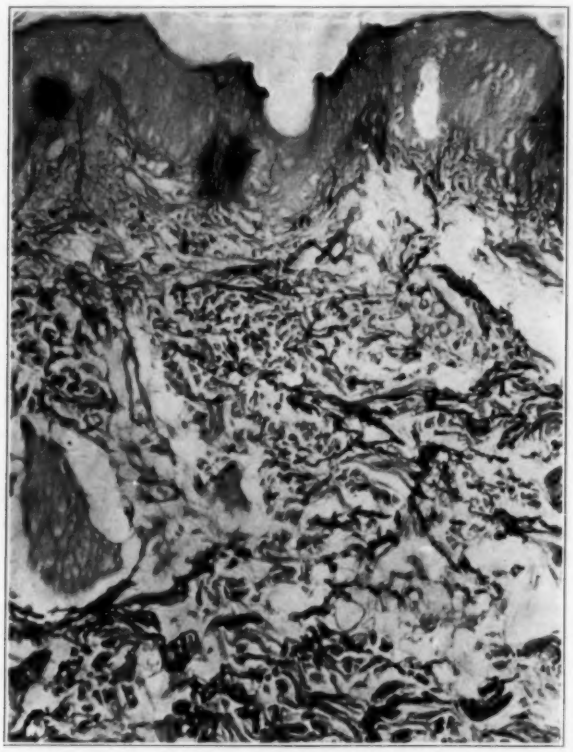

Fig. 2.—Weigert preparation illustrating the scarcity of elastic tissue in the pars papillaris. Elsewhere the elastic fibers are attenuated and distorted.

endothelial cells. The sweat glands were well developed and exhibited nothing abnormal.

Weigert stain showed that the elastic tissue was practically absent in all portions of the section (figs. 2 and 3). At most, only a few disjointed segments appeared in certain portions of the subpapillary region. In deeper parts, such as in the collagen bundles at the level of the sebaceous and sweat apparatus, it was scarcely discernible. On search, a few continuous fibrils could be discovered; but for the most part there were only dots and dashes of the substance.

In none of the sections was there evidence of inflammatory reaction to suggest a preceding inflammatory state which atrophic changes had succeeded.

Clinical Course.—After the child came under our observation, new tumor-like growths appeared. The legs, until then exempt, soon presented three bulging lesions below the right knee and one below the left. New lesions also appeared on the forearms. Antisyphilitic treatment, consisting of eight injections of 0.100 Gm. of bismuth salicylate, failed to alter the eruption. A course of baking was likewise without effect.

An unsuccessful attempt to produce atrophic lesions was made by injecting the patient's own serum intradermally and subcutaneously into the thighs. The internal administration of 10 grains (0.64 Gm.) of potassium iodide three times a day for three weeks failed to result in a lighting up of the lesions as reported in other cases.

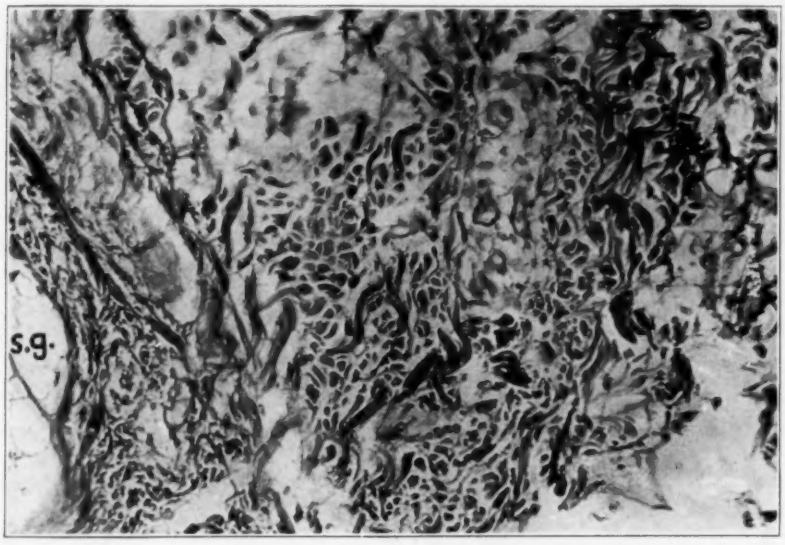

Fig. 3.—Weigert preparation. Focus of anelastosis in the center of the illustration, with a modicum of elastic tissue roundabout. A sebaceous gland is indicated by *s.g.*

COMMENT

This case is unique in that the disease first appeared at the age of 6 years. In twenty-six cases of multiple benign tumor-like new growths of the skin gathered from the literature, of which seven cases were associated with syphilis, the largest number of cases, namely, fourteen, appeared first in the third decade. Three cases occurred between the ages of 10 and 20, two between 30 and 40, one between 40 and 50, and one between 60 and 70. Two patients were described as middle-aged women and one as a male adult; in two instances the age was not given. Among the cases occurring prior to the third decade are: Andrews' case,[5] appearing in a white woman at the age of 18; Kiss-

5. Andrews, G. C.: Atrophia Cutis Maculosa, Arch. Dermat. & Syph. **22:** 1150 (Dec.) 1930.

meyer's case,[6] in a girl, aged 14, and Tobias' case,[7] in which tumor-like growths appeared at the age of 13. The last-named case was presented before the St. Louis Dermatological Society as one of "Multiple Benign Tumor-Like Growths." In the discussion that followed, it was the consensus among those present that the case was one of Recklinghausen's disease. Unfortunately, histologic sections were not presented.

Previous reports have failed to mention the occurrence of a low grade fever in primary macular atrophy. In the case under discussion the temperature ranged between 99 and 100.1 F. consistently during the entire period of our observation. Attempts to explain the mild grade of fever on the basis of a concomitant disease have been futile. The roentgen examination of the chest, the Mantoux series and the cultures of the blood gave normal findings. The laryngeal consultant felt that the ethmoiditis was insufficient to produce the fever; this point of view was supported by the low white blood count. It is possible that the mild fever, associated with a relative lymphocytosis, was indicative of a low grade infection related in some way to the macular atrophy.

In reporting "A Case of Multiple Benign Tumor-Like New Growths of Schweninger and Buzzi" Pusey [2] considered the entire picture to be a congenital defect in the skin characterized by the failure of development of the elastic fibers. The occurrence of this disease in a 6 year old child tended to support this point of view. This conception was especially significant in view of the fact that another congenital defect, mental deficiency, was so common in the child's family; the patient was of borderline mentality.

The rôle of syphilis in this case was uncertain. Although it was known that the mother had a positive Wassermann reaction of the blood at the time the child was born and three years later suffered from a gumma of the nasal septum, the clinical and serologic evidence was entirely negative for congenital syphilis in the patient studied.

238 North Fifth Street.

6. Kissmeyer, A.: Atrophia cutis maculosa, Zentralbl. f. Haut- u. Geschlechtskr. **8**:25, 1923.

7. Tobias: Multiple Benign Tumor-Like Growths, Arch. Dermat. & Syph. **20**:136 (July) 1929.

News and Comment

ADVISORY BOARD FOR MEDICAL SPECIALTIES

The Advisory Board for Medical Specialties has been established for the purpose of coordinating the work of the various examining boards in the specialties and standardizing to a certain extent their methods in the certification of specialists. In these activities are enrolled other organizations already concerned with postgraduate medical education in the specialties. Representatives have been selected from the five examining boards already formed—the American Board of Ophthalmology, American Board of Otolaryngology, American Board of Obstetrics and Gynecology, American Board of Dermatology and Syphilology and American Board of Pediatrics, together with representatives from the Association of American Medical Colleges, the National Board of Medical Examiners, the Federation of State Medical Boards of the United States and the American Hospital Association. The American Medical Association through the Council on Medical Education and Hospitals will, it is hoped, be affiliated with the Advisory Board for Medical Specialties, perhaps in a judicial capacity. The details of this affiliation have not yet been completed.

The officers are: Dr. Louis B. Wilson of Rochester, Minn., president; Dr. J. S. Rodman of Philadelphia, vice president; Dr. Paul Titus of Pittsburgh, secretary and treasurer. The other members of the executive committee are Dr. W. P. Wherry of Omaha and Dr. W. B. Lancaster of Boston.

The Advisory Board for Medical Specialties will doubtless have an important influence on graduate medical education in the specialties and, in addition, a certain amount of influence in an advisory way on undergraduate medical education as well. It will assist in the active investigation and listing of postgraduate training facilities in both the United States and Canada and to a lesser extent abroad. Much of this work has already been done in the undergraduate field in the United States by the Council on Medical Education and Hospitals of the American Medical Association.

It has already been suggested that the time may soon come when the various states will license physicians to practice as specialists and that a certificate from one of the specialty boards will be the basis of such a license. In this connection it is interesting to note that one province in Canada already licenses all of its specialists, and various countries abroad perform a similar function.

It is planned that the next edition of the American Medical Directory will contain information about the various specialty boards which have been formed, as well as indicate in a more graphic way than before the physicians practicing the specialty who are diplomates of these boards. Plans are also made to publish a directory of diplomates which will contain information regarding available postgraduate training facilities together with the general and special qualifications necessary for certification in the various fields. In the last two years there has been a decided trend toward some form of regulation in the special fields, and a greater impetus has been given to the establishment of specialty examining boards. Several other boards are in the process of formation, and in a few years all the recognized specialties will, undoubtedly, be represented by boards.

The lists of qualified specialists already published have come to be extremely useful, not only in the referring of patients from one section to another, but also for the assistance of medical schools, hospitals and similar organizations in selecting properly qualified persons for appointments. There is every reason to believe that the progress of these specialty boards will decidedly increase the quality of specialty service available to the people and thus promote an improvement of medicine in general.

Dermatology is participating in this program by the cooperation of the American Board of Dermatology and Syphilology which was formed in 1932. This board has already held one examination, has issued certificates to approximately 140 dermatologists and is conducting another examination at the meeting of the American Medical Association in June. It is also making a survey of the facilities for postgraduate education in dermatology and syphilology in this country and Canada. Such investigations, in the end, will result in the providing of better instruction than that now given and in the production of better trained and more competent practitioners of our specialty.

DR. BLUMENTHAL RESEARCH PROFESSOR IN DERMATOLOGY

Dr. Franz Blumenthal, professor extraordinary of dermatology and syphilology at the University of Berlin and formerly head of the department in that university, has accepted an invitation to serve as research professor of dermatology at the University of Michigan Medical School for a period of two years. Professor Blumenthal is well known to his American colleagues, many of the younger ones of whom have studied with him. Among his American contemporaries, he will be remembered for his affable and modest demeanor, which has made him a friend as well as a colleague.

Obituaries

JAY FRANK SCHAMBERG, M.D.
1870-1934

American dermatology has been seriously hurt by the recent death of some of its ablest representatives. In quick succession John Lane and Walter Highman have gone, and now we must mourn the death of Jay Frank Schamberg. They were men whom we could ill afford to lose.

Dr. Schamberg had been in failing health for a couple of years, and on March 30 he died of heart disease. He was born in Philadelphia on Nov. 6, 1870, and made his home there throughout his life. He was educated in the Philadelphia schools, and received his medical degree at the University of Pennsylvania in 1893. He served an internship at the University Hospital, where he came under the influence of the great leaders of dermatology in Philadelphia—Duhring, van Harlingen, Stelwagon, Hartzell—and, choosing dermatology as his specialty, he spent, after his internship, a preliminary year in dermatologic study in Vienna, Paris and Berlin. His real development in dermatology, however, came through the influence which surrounded him in Philadelphia, and he was essentially a representative—and a worthy one—of that distinguished Philadelphia school of American dermatology. His affiliations in Philadelphia were desirable from the start, and his ability gave him early recognition. He became professor of dermatology at Temple Medical School and then at Jefferson Medical School and the Philadelphia Polyclinic, which was later affiliated with the University of Pennsylvania as its graduate school of medicine. His professorship at the Graduate School of the University of Pennsylvania was terminated by his death.

Schamberg was greatly interested in the exanthemas, particularly in regard to public health problems, and in 1912 he was appointed a member of the Pennsylvania State Vaccination Board by Governor Tener. The unique background which Schamberg possessed for this study, owing to his expert knowledge of diseases of the skin, gained for him a peculiar distinction in this field. His book "The Acute Contagious Diseases," written in collaboration with William Welch, is one of the best texts on the subject. Always public spirited and militant when necessary in public health problems, he became one of the most effective antagonists of the antivaccinationists.

Schamberg's writings, as attested by the accompanying list of his more important books and papers, covered a wide range of dermatologic subjects. They were characterized by broad scholarship as well as the

fullest knowledge of his specialty, by a strongly developed scientific spirit, originality and common sense and by meticulous care in preparation. One of his early papers, "A Progressive Pigmentary Dermatosis," will perpetuate his name, as the disease is widely known today as Schamberg's disease. In collaboration with Dr. Goldberger of the United States Public Health Service, he discovered the causative mite of "grain itch" and wrote a monograph in 1909 entitled "Grain Itch (Acaro-Dermatitis Urticarioides): A Study of a New Disease in This Country."

JAY FRANK SCHAMBERG, M.D.
1870–1934

Perhaps the most concrete evidence of Dr. Schamberg's achievements is the Research Institute of Cutaneous Medicine in Philadelphia. The story of the founding of this institute testifies to his zeal for research and to his high ideals. A generous patient contributed the first fund for the study of psoriasis. With the outbreak of the World War, Dr. Schamberg and his research associates recognized that there might be an interruption in the importation of arsphenamine. Realizing, furthermore, that the United States might get into the war, Dr. Schamberg, in cooperation with Dr. Raiziss and Dr. Kolmer, worked out a process for the manufacture of the drug. The Federal Trade Commission, recognizing the valuable service the Dermatological Research Laboratories were rendering to American medicine, licensed the laboratories

to operate under the foreign patents on arsphenamine. Without it, the American Army as well as the American people would have been without a satisfactory supply of the drug. The immense value of this foresighted work is well known. The price charged for arsphenamine was about one fourth of the cost of the previously imported product, and large sums were saved the government and hospitals. In spite of the low price asked for the arsphenamine, about $750,000 was realized from its sale and the eventual sale of the laboratories to a large drug manufacturing firm. This entire fund was turned over for the founding of the Research Institute of Cutaneous Medicine, of which Dr. Schamberg acted as director to the time of his death. It was his life's ambition to devote his later years entirely to research—a wish that was never gratified.

Dr. Schamberg was president of the American Dermatological Association from 1920 to 1921; he was chairman of the Section on Dermatology and Syphilology of the American Medical Association from 1928 to 1929, president of the Philadelphia County Medical Society in 1931 and a member of the editorial board of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY from 1927 until his death. He was corresponding member of the Dermatological Society of Denmark, the Dermatological Society of France and the Argentine Dermatological Society.

Schamberg was tall and well proportioned, with black hair and eyes and a handsome, expressive face, was always well dressed, and had courtly manners; he looked the intelligent educated gentleman. He was a polished and fluent speaker, and in discussions, whether in dematology or in other fields, he was notable. With these qualities, he had social attractions which gave him wide popularity.

C. S. W.
W. A. P.

LIST OF BOOKS AND MORE IMPORTANT ARTICLES

A Compend of Diseases of the Skin, first published in 1898, Philadelphia, P. Blakiston's Son & Co., now in the ninth edition.

Acute Contagious Diseases, Philadelphia, Lea & Febiger, 1905. (In collaboration with William Welch.) Republished as Acute Infectious Diseases, Philadelphia, Lea & Febiger. (In collaboration with J. A. Kolmer.)

Diseases of the Skin and Eruptive Fevers, first published in 1908, Philadelphia, W. B. Saunders Company. Out of print.

Treatment of Syphilis, New York, D. Appleton & Company, 1932. (In collaboration with Dr. C. S. Wright.)

Summary of Research Studies in Psoriasis, J. A. M. A. **63**:729 (Aug. 29) 1914.

Desensitization of Persons Against Ivy Poison, J. A. M. A. **75**:1213 (Oct. 18) 1919.

Comparative Studies of the Toxicity of Arsphenamine and Neoarsphenamine, Am. J. M. Sc. **140**:188, 1920.

Laboratory and Clinical Studies Bearing on the Causes of Reactions Following the Intravenous Injections of Arsphenamin and Neoarsphenamin, Arch. Dermat. & Syph. **1**:235 (March) 1920. (In collaboration with J. A. Kolmer, J. W. Raiziss and C. Weiss.)

Studies in the Chemotherapy of Fungus Infections: I. Fungiastatic and Fungicidal Activity of Various Dyes and Medicaments, Arch. Dermat. & Syph. **6**:746 (Dec.) 1922. (In collaboration with J. A. Kolmer.)

The Relationship of Excess of Uric Acid in the Blood to Eczema and Allied Dermatoses, Arch. Int. Med. **32**:203 (Aug.) 1923. (In collaboration with H. Brown.)

Bilirubin Determinations in the Blood as a Measure of Liver Damage in Treatment with Arsphenamins, J. A. M. A. **82**:1911 (June 14) 1924. (In collaboration with H. Brown.)

The Known and the Unknown About Psoriasis, ibid. **83**:1211 (Oct. 18) 1924.

Studies of the Therapeutic Effects of Fever in Experimental Rabbit Syphilis, Arch. Dermat. & Syph. **14**:243 (Sept.) 1926. (In collaboration with A. M. Rule.)

The Use of Gold and Sodium Thiosulphate in the Treatment of Lupus Erythematosus, Arch. Dermat. & Syph. **15**:119 (Feb.) 1927. (In collaboration with C. S. Wright.)

The Effect of Extremely Hot Baths in Experimental Syphilis, Arch. Dermat. & Syph. **17**:322 (March) 1928. (In collaboration with A. M. Rule.)

Some Studies of Calcium Metabolism: Discussion of a New Therapeutic Compound, Calcium Thiosulphate, Tr. Internat. Dermat. Cong., Copenhagen, 1930.

Pemphigus: Recovery Following Long-Continued Colonic Irrigations and Arsenic by Mouth, Arch. Dermat. & Syph. **25**:134 (Jan.) 1932.

The Dietary Treatment of Psoriasis, J. A. M. A. **98**:1633 (May 7) 1932.

Dr. Schamberg's publications numbered over 150.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

RECURRENT EDEMA OF THE LIDS AND CONJUNCTIVA ASSOCIATED WITH DENTAL INFECTION. HUNTER SCARLETT, Am. J. Ophth. **17**:242 (March) 1934.

The author recounts two cases of recurring acute edema of the lids and conjunctiva of one and two weeks' duration, respectively; in both cases an abscess of the apex of a tooth was found which yielded Streptococcus haemolyticus on culture. Removal of this focus of infection was followed in both cases by disappearance of the edema, without local treatment.

SYPHILIS OF THE CLAVICLE. FRANCIS M. CONWAY, Ann. Surg. **99**:290 (Feb.) 1934.

The author describes three cases of syphilitic lesions of the clavicle, two of which presented pathologic fractures. He states that the criteria of history, roentgenologic findings, Wassermann reaction and response to antisyphilitic therapy should be employed in the diagnosis of the condition, which must be differentiated from sarcoma and tuberculosis and in the hyperostotic form from Paget's disease.

WIEDER, Milwaukee.

ON SOME ASPECTS OF PSORIASIS. J. F. BURGESS, Canad. M. A. J. **30**:165 (Feb.) 1934.

In briefly reviewing the various theories as to the etiology of psoriasis, Burgess refers especially to the work of Bizzozero on the phenomenon of Koebner, namely, that during a certain period in the evolution of psoriasis typical linear psoriasis may be evoked as a result of cutaneous excoriations. Bizzozero determined that the traumatic stimulus acts directly on the papillary layer and that a certain incubation period is present before the development of psoriasis, a period which varies for different persons. This suggests that in psoriatic patients some biochemical substance is formed which comes into contact with the basal cells of the epidermis through the blood or lymph stream, and by its action interferes with the normal evolution of epidermal cells. A person never acquires permanent immunity to this reaction; there are recurrences of the disease, probably due to the influence of associated conditions, such as metabolic disturbances, constitutional dyscrasias (e. g., gout, anemia and arthritis) and perhaps endocrine disturbances. Burgess then considers the treatment of psoriasis, using the following classification: (1) acute early psoriasis; (2) recurrent generalized psoriasis; (3) fixed localized psoriasis; (4) psoriasis of the nails, and (5) interval therapy. In suitable cases of recurrent generalized psoriasis encouraging results have been obtained by intravenous injections of gold sodium thiosulphate in large doses in combination with local applications. The author has had many failures, especially in cases with sparse, fixed areas of involvement. The patient may become immune to the drug after prolonged use, and recurrences are not prevented. The treatment recommended for the other varieties of psoriasis is similar to that mentioned in most textbooks. For interval therapy Burgess uses ultraviolet radiation, which in his experience helps to prolong the period between attacks.

IODERMA FROM AN ASTHMA REMEDY. D. E. H. CLEVELAND, Canad. M. A. J. **30**:180 (Feb.) 1934.

Typical fungating ioderma developed in a man who, for years, had taken "Felsol," a powder containing among other substances an iodine derivative of antipyrine.

SUPERFICIAL ABDOMINAL GANGRENE AS A COMPLICATION OF VARICELLA. T. R. NICHOLS, Canad. M. A. J. **30**:297 (March) 1934.

The gangrenous process spread rapidly, despite surgical intervention, and the patient, a girl aged 11, died within a few days. Staphylococci were found in a smear of the pus.

RATTNER, Chicago.

DERMATITIS DUE TO WOODS. FRANCIS E. SENEAR, J. A. M. A. **101**:1527 (Nov. 11) 1933.

Senear reports a case of dermatitis due to contact with the dust of yew wood from archery bows. The literature is reviewed for reactions resulting from contact with woods, and these are found to include dermatitis venenata, morbilliform and scarlatiniform eruptions, urticaria and symptoms of involvement of the mucous membranes and the respiratory system. The cutaneous and general reactions are regarded as allergic. The reprints include a table listing woods causing dermatitis and their common uses.

CORNEAL ULCERATION FOLLOWING USE OF LASH-LURE. A. W. MCCALLY, A. G. FARMER and E. C. LOOMIS, J. A. M. A. **101**:1560 (Nov. 11) 1933.

Following a single application of Lash-Lure to her eyelashes a woman had severe conjunctivitis and acute dermatitis of the face. This soon led to corneal ulceration and after a prolonged course resulted in corneal opacity and nearly total loss of vision in both eyes.

DIVIDED DOSES OF TYPHOID VACCINE IN THE FEVER THERAPY OF NEUROSYPHILIS. J. R. DRIVER and H. C. SHAW, J. A. M. A. **101**:2016 (Dec. 23) 1933.

Higher temperatures may be obtained by injecting a second dose of typhoid vaccine intravenously when an initial rise in temperature has resulted from the first dose given from two to four hours previously. The divided dose method is an excellent and easily available substitute for malaria treatment for neurosyphilis.

USE OF PHENYLMERCURIC NITRATE IN TINEA AND YEAST INFECTIONS OF THE SKIN. B. LEVINE, J. A. M. A. **101**:2109 (Dec. 30) 1933.

Phenylmercuric nitrate is presented as a valuable drug for the treatment of fungous infections of the skin. Of 262 cases studied the author reports cures in the 205 which were carefully followed, including cases of interdigital saccharomycosis and of tinea of the feet, hands, groins and axillae, one case of generalized tinea corporis of seven or eight years' duration and one case of tinea barbae which was cured in ten days. The author states that in the remaining 57 cases there was definite improvement but they were not followed to completion of the treatment.

CONTACT ECZEMA DUE TO CLOTHING. F. A. SIMON and F. M. RACKEMANN, J. A. M. A. **102**:127 (Jan. 13) 1934.

A patient had recurrent attacks of dermatitis which were caused by contact with dyed socks, a blue serge suit, the collar of an overcoat, a hat band, garters and other articles of clothing and with the upholstery of automobiles and furniture. Patch tests were performed with undyed wool, cotton and silk, mordants used in dyeing and many commercial dyes; there were positive reactions to many of the dyes but to no other substances. Scratch tests were all negative, and attempts at passive transfer of the sensitivity were unsuccessful.

TRAUMATIC EPITHELIAL CYSTS OF THE SKIN. M. S. WIEN and M. R. CARO, J. A. M. A. **102**:197 (Jan. 20) 1934.

Three cases of traumatic epithelial cysts of the skin are reported, with histologic examination in two. Such cysts occur on sites exposed to trauma and usually result from injury by blunt or tearing instruments. They are usually formed from a bit of epidermis which has been torn from the surface and implanted in the corium, but they may originate from injured deeper epithelial structures.

BILATERAL NECROSIS OF THE CORNEA FOLLOWING THE USE OF HAIR DYE ON THE EYEBROWS AND LASHES. C. T. MORAN, J. A. M. A. **102**:286 (Jan. 27) 1934.

Severe conjunctivitis and dermatitis of the face followed a single application of Godefroy French Hair Coloring (Larieuse) to the eyebrows and lashes. A corneal ulcer appeared in each eye, and the one in the right eye perforated in spite of careful treatment. A scratch test on the arm showed the patient to be very sensitive to paraphenylendiamine. Temporary removal of the eyebrows and lashes is suggested as a valuable aid in treatment.

GENERALIZED ANGIOMATOSIS (TELANGIECTASIA). J. F. MADDEN, J. A. M. A. **102**:442 (Feb. 10) 1934.

The author divides multiple telangiectasia into the following three types: primary telangiectasia, including hereditary hemorrhagic telangiectasia; secondary telangiectasia, dependent on constitutional disease or pregnancy, and nevoid telangiectasia. Cases representing all three types are reported, and the literature is reviewed.

CARO, Chicago.

EPHEDRINE DERMATOSES: CLINICAL AND EXPERIMENTAL STUDY OF A PERSONAL CASE WITH A REVIEW OF THE LITERATURE. E. W. ABRAMOWITZ and M. H. NOUN, Brit. J. Dermat. **45**:225 (June) 1933.

The authors review the literature on cutaneous eruptions attributed to ephedrine, add a case of their own and compare some of their experiments with those undertaken by others to determine the specific sensitizing agent.

ERYSIPELAS AND MYCOSIS FUNGOIDES. H. MACCORMAC, Brit. J. Dermat. **45**:237 (June) 1933.

Two cases are reported to illustrate the beneficial effect of an attack of erysipelas on mycosis fungoides. In both cases the disease was severe and rapidly progressive, and the author feels that it would have led to a fatal issue had not an accidental infective process intervened at the critical stage. The first patient was a woman, aged 59; tumors of mycosis fungoides had appeared seventeen years before, and erysipelas developed twelve years before. The second patient was a man, aged 52, who was first seen in June, 1932, with rapidly progressing mycosis fungoides d'emblée, which was favorably influenced by an attack of erysipelas in September, 1932.

THE QUESTION OF IRRADIATION BY X-RAYS AS A CAUSE OF SARCOMA. D. W. MONTGOMERY and J. D. VIECELLI, Brit. J. Dermat. **45**:241 (June) 1933.

A physician, aged 68, for over a year was under treatment for growths occurring in skin profoundly affected by x-rays as a result of treatment for sycosis vulgaris about thirty years before. Two tumors developed. One, on the cutaneous surface of the left ala nasi, was shown to be a cuboid cell epithelioma. The other was deeply situated in the substance of the left side of the upper lip, and after excision the sections revealed a quite cellular connective tissue type of tumor which was growing. In many fields the cells resembled those of spindle cell sarcoma;

these were definitely not infiltrative cells but those of the locality itself and were evidently the ones causing the increase of growth.

TREATMENT OF PSORIASIS BY THE INJECTION OF SCALES. N. W. WRONG, Brit. J. Dermat. **45**:244 (June) 1933.

The technic of Toma (*Ann. de dermat. et syph.* **7**:1110, 1931) was used, with the modification that the scales were weighed and 1 cc. of sterile physiologic solution of sodium chloride was added to each 10 mg. of scales. Ten cases are reported. In one the eruption entirely cleared; in five there was definite improvement; in one, slight improvement, and in four, no improvement.

A CASE OF PRIMARY LEUCOSARCOMA OF THE SKIN. W. N. GOLDSMITH, Brit. J. Dermat. **45**:281 (July) 1933.

A man, aged 65, had copper-colored or plum-colored infiltrated papules, varying in size to 2 cm. in diameter, chiefly on the forehead and cheeks. There were also flat infiltrations on the lower limbs and a large fungating tumor arising abruptly on the outer side of the left thigh just above the knee. The necropsy report and a description of histologic sections from the skin, spleen and liver are presented. The group of diseases to which this condition belongs is classified and discussed. The author concludes that the case had the general characteristics of Sternberg's leukosarcoma. It differed from classic leukosarcoma in that (*a*) though the tumors were composed mainly of the usual monocytes, the blood leukocytes consisted predominantly of small lymphocytes; (*b*) there were no hemorrhages, and (*c*) the primary tumor originated in the skin and was unusually malignant. Recent work points to the probability that at least three conditions, known as lymphatic leukosis, leukosarcoma and lymphosarcoma, are manifestations of the same disease and that the variations depend on differences in the persons attacked. The case reported, with its combination of small lymphocytes and monocytes, is considered to support this view. The nature and origin of the monocytes are discussed, and a hypothesis as to the pathologic sequence of events is suggested. Four clinical photographs and a photomicrograph are presented.

CELERY ITCH: DERMATITIS DUE TO CELERY IN VEGETABLE CANNING. S. A. HENRY, Brit. J. Dermat. **45**:301 (July) 1933.

The discussion is based on information obtained from a study of twenty-two cases occurring in the vegetable-canning industry in England and is summarized as follows:

"1. A form of dermatitis confined to the upper limbs, mainly bilateral, but tending to commence more frequently on the left side than on the right, and associated with itching, occurred amongst workers preparing celery for canning during the autumn of 1932.

"2. Approximately 4 per cent of the workers were affected.

"3. The great majority (83.6 per cent) of those affected were under 30 years of age.

"4. Transference to other work with treatment at the ambulance room was the usual procedure adopted, and by this method approximately 41 per cent were completely cured within one week and 86 per cent in 4 weeks.

"5. In only 4 (18.1 per cent) was there total disability necessitating absence from work for periods varying from 2 to 53 days (average 25 days).

"6. It is suggested that the main causative factor is limonene, a hydrocarbon of the terpene series and a constituent of celery oil, water, friction and individual susceptibility playing their respective rôles as preparatory causes.

"7. The preventive measures adopted consisted of transferring the patient to other work, and the application to the skin, of those not affected, of a suitable oil before commencing work."

A Peculiar Form of Purpura. A. Piney, Brit. J. Dermat. **45**:309 (July) 1933.

A case is reported in a boy, aged 17, who after a sudden attack of gastrointestinal disturbance presented a peculiar eruption of purpuric spots and vesicles in crops, each exacerbation being associated with a peculiarly strong fecal exhalation from the skin. Well marked monocytosis was present in the blood in the early stages of the disease. There was albuminuria late in the course, after the fever subsided. In spite of the collapsed condition of the patient at the time of admission to the hospital there was complete recovery. A plate illustrating the lesions on the right hand and foot accompanies the article.

Wien, Chicago.

Hypodermolithiasis. J. Patterson Ross, Brit. M. J. **1**:234 (Feb. 10) 1934.

The author limits the term hypodermolithiasis to cases in which subcutaneous calcareous nodules are formed in the absence of antecedent lesions of the skin, such as cysts, tumors, or tuberculous foci. The lesions described are easily differentiated from gouty tophi, for tophi are not opaque to the x-rays. He reports three cases, in women aged 28, 52 and 62, respectively. Analysis of the nodules in one of the cases revealed them to be mixtures of calcium phosphate and calcium carbonate, chiefly calcium phosphate. There was nothing in the cases to suggest a disturbance of calcium metabolism. The condition appeared to be purely a local disorder resulting from impairment of the blood supply and malnutrition of the subcutaneous tissue. The patients were all women whose peripheral blood vessels were unduly susceptible to cold, and the deposits occurred in the portions of the upper extremities which are naturally the coldest. Ross reviews briefly the various theories which explain the chemical reactions underlying calcification. He concludes that, whatever the true explanation of calcification is it is necessary to postulate tissue degeneration; in the case of hypodermolithiasis such degeneration may well be the result of local vascular disorder, which if recognized early may be arrested by sympathetic ganglionectomy. He has not had an opportunity to carry out this treatment in any of his cases.

Rattner, Chicago.

Human Anthrax: Its Effective Treatment with the Organic Arsenic Preparations. H. A. Spencer, J. Trop. Med. **37**:9 (Jan. 1) 1934.

Spencer reports a few cases of anthrax in adults and children, the infection being caused by contaminated meat or hides of goats and oxen.

Neoarsphenamine was given in most cases, one injection of 0.6 Gm. usually being sufficient, but for children 3 grains (0.18 Gm.) of sodium cacodylate produced equally good results.

Injections of antianthrax serum were followed by similar results.

Jamieson, Detroit.

The Optic Nerve and Pentavalent Arsenicals. Sezary and P. de Font-Reaulx, Ann. de dermat. et syph. **4**:289 (April) 1933.

All the factors bearing on injury to the optic nerve as a result of treatment with the pentavalent arsenicals are discussed in detail, and the writers are led to the following conclusions: 1. Certain pentavalent arsenicals, such as atoxyl and arsacetin, have a toxic affinity for the optic nerve, but this is due to their chemical composition and not to their arsenic content. 2. Large doses, even when given infrequently, are dangerous; the same total dosage can be reached as readily with smaller single doses without the risk of ocular accident. 3. The terrain offered by the organism is of great importance. Ocular complications are favored by the presence of such a condition as renal or hepatic insufficiency, alcoholic intoxication or a lesion of the central nervous system.

There is an occasional case of damage of the optic nerve which can apparently be explained only on the ground of idiosyncrasy in the patient, but such a case is only an exception proving the rule that in most instances an important predisposing cause is present.

PSEUDOBROMODERMA OF BROCQ. K. BEINTEMA, Ann. de dermat. et syph. **4**:399 (May) 1933.

In 1909 Brocq presented a new disease which he called "pseudobromoderma" because of its resemblance to the eruption produced by bromides. The cause of the condition could not be demonstrated. In 1918 he described three additional cases but was unable to throw any light on the etiology. Beintema now adds two cases. He was able to investigate one thoroughly, and he presents rather convincing proof of the mycotic nature of the condition. A fungus was isolated which seems to be a new species belonging to the transitory group between the arthrospores and the blastospores, a group for which Ota, in 1924, proposed the name Parendomyces. In honor of the great master this organism is named Parendomyces Brocquii. A cutaneous allergic reaction was demonstrated, the lesions could be reproduced in rabbits, and all Koch's postulates seem to have been satisfied. The disease is systemic, probably originating in the lungs, the skin lesions being analogous to the well known "ids." Potassium iodide proved to be a near specific, as expected. From the excellent cuts accompanying the text one would certainly think of bromoderma as the most likely clinical diagnosis.

GANDY, Houston, Texas.

MUCOCUTANEOUS LEISHMANIASIS OF THE NASAL CAVITY. G. FALCHI, Gior. ital. di dermat. e sif. **74**:1109 (Oct.) 1933.

Mucocutaneous manifestations of leishmaniasis are not observed exclusively in Central and South America, nor are they always due to Leishmania americana. Falchi reports a case of an ulcer of the right nostril and septum in a man aged 40, a native of Italy who had never been abroad. The diagnosis was confirmed by the presence of Leishmania in the smears and in the tissues.

LICHEN NITIDUS. MARIO ARTOM, Gior. ital. di dermat. e sif. **74**:1241 (Oct.) 1933.

Lichen nitidus and papulonecrotic tuberculids occurred in a young girl suffering from pulmonary tuberculosis. The author concludes that lichen nitidus should be definitely separated from lichen planus and considered as a tuberculid.

CUTANEOUS GENERALIZED LYMPHOSARCOMATOSIS SECONDARY TO A PRIMARY TUMOR OF THE LYMPHATIC GLANDS OF THE GROIN. A. AMBROGIO, Gior. ital. di dermat. e sif. **74**:1287 (Oct.) 1933.

This case was classified as one of lymphosarcoma or atypical polymorphous cell sarcoma of Darier. Differential diagnosis from malignant lymphogranulomatosis of Paltauf and Sternberg, mycosis fungoides, lymphadenoma, sarcomatosis of Spiegler and Fendt and Kaposi's sarcoma is considered. The tumors were generalized over the cutaneous surface and were also found in the lymph glands, the liver and the endocardium. They were made up of a reticulum of very fine fibrils irregularly interlaced. This reticulum was filled with polymorphous cells, some elongated and fusiform, others round or stellate and still others shaped like tacks or rackets or polygonal. These cells had large vesicular nuclei with a lax chromatin reticulum and a granular protoplasm. Many cells were multinucleated, and karyokinetic figures were common. Giant cells with polylobulated nuclei, resembling megakaryocytes, were observed. Numerous blood vessels were seen in the midst of the tumors.

VERMIFORM CUTANEOUS ATROPHY. A. GLINGANI, Gior. ital. di dermat. e sif. **74**:1319 (Oct.) 1933.

The author reports a case of atrophoderma of the face appearing in vermiform striae, which was neither preceded nor accompanied by folliculitis, comedones or erythema. Histologically there were atrophy of the epidermis, degeneration of the elastic tissue, thickening and sclerosis of the connective tissue bundles and multiple foci of moderate perifollicular inflammation. The etiology remained unknown. The patient was a youth aged 18, in good general health.

INFLUENCE OF SODIUM CHLORIDE IN EXPERIMENTAL TUBERCULOSIS OF THE RABBIT. T. G. BERTACCINI, Gior. ital. di dermat. e sif. **74**:1469 (Dec.) 1933.

Thirty-six rabbits were inoculated intradermally with a culture of bovine tubercle bacilli. A number of these animals were kept on a diet rich in sodium chloride during several months, and the rest were kept on a salt-free diet. The clinical evolution seemed to prove that the animals kept on a salt-free diet had a better defense against infection and that the cutaneous lesions were less intense and less likely to spread. Histologic studies showed that in the subjects on a salt-free diet the connective tissue reaction was more marked and there was a greater tendency to surround and smother the active tuberculous lesions.

SENEAR-USHER'S PEMPHIGUS. G. F. CHIALE, Gior. ital. di dermat. e sif. **74**:1487 (Dec.) 1933.

The author reports a case which seems to belong in the syndrome described by Senear and Usher. He concludes that the condition is not a transitional form between pemphigus and lupus erythematosus but rather a variant of classic pemphigus vulgaris.

AMYLOID DEGENERATION OF THE SKIN. G. SANNICANDRO, Gior. ital. di dermat. e sif. **74**:1499 (Dec.) 1933.

The cutaneous manifestations of an alteration of the protein metabolism which causes the deposition of an amyloid substance in the tissues are many and varied. Amyloidosis of the skin may be primary and the only manifestation of the disorder or may exist together with or consecutive to amyloidosis of the internal organs. The most common clinical cutaneous manifestations are pseudoscleroderma or sclerodermiform amyloidosis, but in some cases hemispheric, semitransparent papules constitute the most prominent feature. Primary cutaneous amyloidosis is characterized by its localization on the legs, forearms and back, by intense pruritus and by clinical symptoms of the type of lichen simplex chronicus, lichen planus, prurigo and lichenification. The histologic picture is characteristic. The amyloid substance is localized in the upper part of the corium, and there are a moderate inflammatory reaction and hyperkeratosis. The most characteristic change is the presence of fissures between the epidermis and the corium. Atrophy of the epidermis is seen in the late stages. Primary amyloidosis of the skin is the result of degeneration of the supporting tissues of the corium, particularly of the elastic tissue. The author reports his findings in ten cases of this condition.

THALLIUM ACETATE AND THALLIUM SALICYLATE: EXPERIMENTAL BIOLOGIC DOSAGE. GINO PELI, Gior. Ital. di dermat. e sif. **74**:1613 (Dec.) 1933.

Thallium acetate has proved more toxic than thallium salicylate in the author's experience. He concludes that roentgen therapy should be preferred to the administration of thallium in the treatment of tinea of the scalp. Thallium salicylate should be preferred to thallium acetate if thallium is used, which should be only in the case of very small children. The minimum lethal dose of thallium salicylate for new-born guinea-pigs was found to be 22 mg. per kilogram of body weight, and the minimum alopecic dose was 12 mg. per kilogram.

SYPHILIS AND TUBERCULOSIS. ALFREDO NARIO, Rev. méd. latino-am. **19**:240 (Dec.) 1933.

On the basis of his studies of one hundred and twenty cases of syphilis and tuberculosis the author concludes that syphilis does not predispose the patient to tuberculosis, that recently acquired syphilis aggravates existing tuberculosis, that syphilis of long standing has no influence on the evolution of tuberculosis and that antisyphilitic treatment does not affect favorably or unfavorably the course of tuberculous infection of the lungs.

IS A PROTECTIVE MECHANISM DEVELOPED BY THE NERVOUS SYSTEM DURING THE SECONDARY STAGE OF SYPHILIS? EARLY TREATMENT OF SYPHILIS AND FINDINGS IN THE SPINAL FLUID. JOSE LUIS CARRERA, Rev. sud-am. de endocrinol. **17**:1 (Jan. 15) 1934.

The author comments on the theory that has been expounded by some syphilologists concerning the development of a protective mechanism of the nervous system during the early periods of syphilis and on the supposed interference of antisyphilitic treatment with this hypothetic defensive process. There is no evidence that the appearance of secondary cutaneous eruptions creates an increased resistance to infection on the part of the nervous system. There is no evidence, moreover, that the development of cutaneous inflammations diminishes the severity of syphilitic infection. The supposed favorable influence of postarsphenamine dermatitis on the course of syphilis has been proved not to exist. The author advocates the use of intensive treatment as early as possible as a guarantee against the future development of neurosyphilis. In seventy-three cases in which the patients were treated early and intensively, the spinal fluid remained normal after three years except in six instances. In these the abnormalities found were minor and easily controlled by further antisyphilitic treatment.

PARDO-CASTELLO, Havana, Cuba.

THE MECHANISM OF THE URTICARIAL IDIOSYNCRASY TO EGG WHITE IN THE ECZEMATOUS CHILD. WERNER JADASSOHN and FRITZ SCHAAF, Ztschr. f. Immunitätsforsch. u. exper. Therap. **79**:407, 1933.

Dialysates of egg white are known to be urticariogenic in the allergic eczematous child. Opinions differ as to whether the reacting substance is protein or, as Jadassohn and Schaaf and others maintain, nonprotein. When the proper technic is employed, no protein substances pass into the dialysate. An analysis of the reports to the contrary discloses faults in the technic of dialyzing or in the methods of determining the presence of protein substances in the dialysates. The comparison, by means of the Prausnitz-Küstner technic, of the urticariogenic potency of egg white and that of dialysate revealed that the latter reacted in quantities which could not contain the minimum concentration of protein found necessary in quantitative tests with egg white. By means of the Prausnitz-Küstner technic it was possible to demonstrate that chicken egg white contains at least two antigenic substances; one of them is also present in duck egg white. Both pass through the dialyzing membrane. The blood serum of eczematous children with urticarial hypersensitiveness to egg white contains substances which can neutralize the urticariogenic properties of egg white. By means of the Schultz-Dale technic trichophytin produced anaphylactic phenomena in dilutions which made it probable that that reaction was not due to protein substances. Jadassohn and Schaaf conclude that urticarial hypersensitiveness and anaphylaxis are closely related.

THE CURABILITY OF LATE SYPHILIS IN RABBITS AND THE QUESTION OF IMMUNITY. P. MANTEUFEL and K. HERZBERG, Ztschr. f. Immunitätsforsch. u. exper. Therap. **79**:482, 1933.

Two groups of twenty rabbits were used for the experiment; one group had had a syphilitic infection, and the other frambesia tropica. A reinfection with the homologous parasites was asymptomatic. Several months after the reinfection the animals were subjected to a thorough treatment with neoarsphenamine. The effect of the treatment was checked by means of glandular transplants which were negative in the cases tested. The rabbits were then reinfected for the third (or in some instances for the second) time. The infection was again asymptomatic. Five months later the rabbits were killed and their organs transplanted into the testicles of healthy rabbits. Only twenty-one rabbits survived the entire experiment, and the organs of thirteen of these were free from spirochetes, while the remaining eight still showed the presence of the disease. The thirteen rabbits were considered as immune by Manteufel and Herzberg. That interpretation is contrary to both hypotheses of Kolle, who maintains: (1) that late syphilis in rabbits cannot be cured with arsphenamine, and (2) that in syphilis of rabbits there develops only a "mono-immunity" against the homologous strain as contrasted with the pan-immunity which develops in human syphilis. Cross-experiments failed to furnish a means of biologic differentiation between Spirochaeta pallida and Spirochaeta pertenuis.

DAVIDSOHN, Chicago. [ARCH. PATH.]

Society Transactions

MANHATTAN DERMATOLOGIC SOCIETY

M. B. Parounagian, M.D., *Secretary*

April 11, 1933

Fred Wise, M.D., *Chairman*

Cutaneous Horn and Epithelioma. Presented by Dr. David L. Satenstein.

An Italian woman, aged 76, about six months ago noticed a small nodule on the vermilion border of the lower lip. It caused no subjective symptoms but gradually increased in size. She received no treatment. The conical lesion extends outward from the vermilion border about 1½ inches (3.77 cm.). It is sharply margined, and dull gray at its tip, which is elevated 1 inch (2.5 cm.). The base is surrounded at its border by an excoriated zone. There is little infiltration of the lip, and there are no palpable lymph nodes anywhere. The patient is from the clinic for diseases of the skin of the New York Post-Graduate Medical School and Hospital.

DISCUSSION

Dr. Ludwig Oulmann: There is no doubt that the diagnosis is correct. These cases easily develop into cancer, although there is no sign of a malignant process in this case.

Dr. George M. MacKee: I agree with those who think that squamous cell epithelioma is already present. There is a margin of infiltration at the base producing a rolled-edge appearance. I should advise scalpel excision. The lesion is suitable for such treatment, and the tissue can then be examined microscopically. I believe that the degree of malignancy is comparatively low, and I do not think that the lesion has become invasive.

Dr. Howard Fox: The lesion is of interest because of its large size and comparatively short duration. A similar lesion has been recorded as being a foot long and an inch thick. If this particular lesion is not already malignant at the base, it will later become so and should now be treated as an epithelioma.

Dr. Andrew J. Gilmour: I think that epithelioma is already present.

Dr. Mihran B. Parounagian: I have seen only one case of horn, which was probably four or five times larger than this lesion. The patient was a man, aged 90; when the horn was removed, the base of it showed cancer.

Dr. David L. Satenstein: I wish to emphasize the speed of the growth. The whole lesion grew within the last six months. Acanthotic keratotic lesions are not common in females; there is a possibility of recent development of malignant changes at the base.

Note.—Subsequent microscopic examination revealed early stages of malignancy.

Pityriasis Rosea or Lichen Planus (?). Presented by Dr. Max Scheer.

E. G., a woman, aged 30, from the clinic for diseases of the skin of the New York Post-Graduate Medical School and Hospital, was presented at the New York Academy of Medicine on Tuesday, April 4, 1933. Opinion was divided as to whether the diagnosis was pityriasis rosea or lichen planus. The results of biopsy, made on April 1, 1933, were reported by Dr. Satenstein, who stated that the condition was a quiescent process similar to neurodermatitis.

DISCUSSION

DR. HOWARD FOX: At the present time I can see no evidence whatever of lichen planus. The diagnosis of pityriasis rosea seems probable.

DR. GEORGE M. MACKEE: It appears to be a dermatitis in which at present, the features are not particularly characteristic of any entity, but it does resemble pityriasis rosea more than any other condition.

DR. MIHRAN B. PAROUNAGIAN: I should favor the diagnosis of lichen planus rather than that of pityriasis rosea, because of the bright red appearance and the shining papules.

DR. MAX SCHEER: The lichenoid lesions are increasing in number. I have never seen pityriasis rosea with lichenoid lesions.

POIKILODERMA ATROPHICANS VASCULARE. Presented by DR. MIHRAN B. PAROUNAGIAN.

Mrs. L. S., aged 31, first noticed a pinkish, nonitching eruption on the right arm one year ago; later a similar condition appeared on the left forearm. While these lesions had become darker, a similar eruption had developed on the lower extremities, starting at the buttocks and spreading downward to the feet. At no time was there any itching, but occasionally small, superficial, crusted sores developed; these were painful and itchy, and they required as long as eight weeks to heal.

The patient had a tonsillectomy sixteen years ago, and the removal of an unruptured ectopic pregnancy two years ago. She attended the clinic for diseases of the skin of the New York Post-Graduate Medical School and Hospital, where biopsy of a specimen from the right thigh confirmed the diagnosis. The basal metabolic rate was normal. Diseased tonsils were found. The patient was examined in the capillary clinic, and a report was made that in the beds of the finger nails the capillaries were essentially normal; in the areas of normal skin, the capillary loops were normal in number and in form. In the discolored areas, the same number of loops were present, but they were extremely tortuous, and around certain loops there was an extravasation of blood.

The lesions are distributed chiefly over the arms, forearms, buttocks, thighs and legs. There are also lesions on the back, over the scapulae and on the lower part of the abdomen and the dorsa of the hands and feet. There are no lesions in the mouth or on the palms and soles. They vary from pale pink to deep purple, and many have a distinctly coppery hue. They are of indefinite form, usually small and punctate, here and there pea-sized, but so closely packed that the skin has a mottled appearance. They have, in general, the appearance of intradermal, local hemorrhagic areas in a cutis which, in places, seems remarkably transparent. A few lesions are macular, slightly raised, and faintly pinkish and have a fine furfuraceous scaling.

DISCUSSION

DR. GEORGE M. MACKEE: While the eruption does not present all the characteristics of poikiloderma, I believe that essential generalized telangiectasia can be ruled out and a diagnosis of poikiloderma established. Later, when the eruption is older, there are likely to be more atrophy, pigmentation, depigmentation and other features that make poikiloderma resemble chronic radiodermatitis.

DR. DAVID L. SATENSTEIN: The condition is recent. Atrophy will result later. I accept the diagnosis of Dr. Parounagian.

DR. HOWARD FOX: I agree with the remarks of Dr. MacKee. From time to time we see cases which present some of the manifestations of Jacobi's disease but which are not typical. At all events they do not present a striking similarity to radiodermatitis. Such cases, however, should probably be classed as poikiloderma atrophicans vasculare.

DR. LUDWIG OULMANN: This is a recent case, and it would not show the signs which an older one would. A case I presented two years ago has progressed very much, and I think that in time the symptoms in this case will be similar.

DR. FRED WISE: I agree with the diagnosis and with the opinion of those who believe that this condition will progress to atrophy. Pancreatic extract has allegedly been used successfully by Sellei of Budapest. A trial of that treatment should be made with this patient.

PITYRIASIS RUBRA PILARIS. Presented by DR. MAX SCHEER.

G. G., a man, white, aged 35, born in the United States, came to the clinic for diseases of the skin of the New York Post-Graduate Medical School and Hospital, with the complaint of a rash of ten weeks' duration. The face, shoulders, arms and upper parts of the chest and back present diffuse erythrodermia, sharply defined with, in some cases, a surface feeling like a nutmeg grater. On other parts there is a branlike scaling of the lesions. There are areas of normal skin intervening. On both elbows are typical follicular acuminated papules covered with fine scales. Follicular, horny plugs are present over most of the proximal phalanges. The patient states that he had a similar attack eighteen years ago.

DISCUSSION

DR. ISADORE ROSEN: I am inclined to disagree with the diagnosis as presented. I believe that the patient is suffering from some form of chronic dermatitis due to external causes. His occupation, which involves contact with oils and other greases, may be responsible for the generalized eruption.

DR. GEORGE M. MACKEE: I do not agree with the diagnosis of pityriasis rubra pilaris, but I cannot definitely rule out that condition at present. The distribution and the sharp margins which in places are conspicuous contraindicate a diagnosis of dermatitis venenata. There is considerable folliculitis on the thighs and fingers. Dermatitis due to arsenic or to some other heavy metal must be considered, but the most probable diagnosis is dermatitis venenata caused by petroleum products, tar or some such substance.

DR. HOWARD FOX: I should rule out pityriasis rubra pilaris because there is no scaling of the scalp and no characteristic keratotic thickening of the palms.

LUPUS ERYTHEMATOSUS DISSEMINATUS (?). Presented by DR. ANDREW J. GILMOUR.

A man, aged 49, married, came to the Cornell Clinic in the service of Dr. Schwartz on Oct. 11, 1932, for treatment of a small patch of lupus erythematosus beneath the right eye of two years' duration. He received intravenous injections of gold sodium thiosulphate in doses of 25 mg. at the first, of 50 mg. at the second and of 100 mg. at each of the seven following treatments. The injections were given at intervals of about one week, from October 11 to November 29. On Dec. 6, 1932, because of the presence of small raw red spots in the mouth, the injections of gold sodium thiosulphate were discontinued. (The patient had many gold caps on the teeth.) A smear showed the presence of Streptococcus haemolyticus. The patient had no rise of temperature and did not feel ill, but the throat felt sore for a few days, and warm food burned more than normally.

As the throat did not give any further trouble, the medication was resumed after two months, with 50 mg. of gold sodium thiosulphate. After the fifth injection, the last three of 100 mg., a slight scaling, red rash appeared and has gradually increased. There is an erythematous rash of small patches, none over an inch in diameter, on the trunk and extremities. Some patches are scaly and resemble pityriasis rosea; some have a slight dry crust as if there had been

a small patch of vesicles. On the trunk are several hyperkeratotic follicles in patches. It is the opinion of Dr. Gilmour that the eruption is probably a dermatitis due to the medications with gold preparations or pityriasis rosea.

DISCUSSION

DR. MIHRAN B. PAROUNAGIAN: I am inclined to accept the diagnosis of dermatitis due to gold sodium thiosulphate rather than that of pityriasis rosea. I do not believe that the absence of the constitutional symptoms excludes the diagnosis of dermatitis due to gold sodium thiosulphate.

DR. J. FRANK FRASER: The clinical picture does not conform to that of pityriasis rosea; there is follicular keratosis, which is not seen in pityriasis rosea. I should suggest the diagnosis of lupus erythematosus. A biopsy might confirm this diagnosis.

DR. HOWARD FOX: It is difficult to decide whether this is lupus erythematosus disseminatus, activated by medication with gold preparations, or whether it is simply a medicinal dermatitis. My impression is that the latter alternative is the more probable one.

DR. GEORGE M. MACKEE: The case is puzzling. I have never seen dermatitis caused by gold or arsenic begin exactly like this. I think that we can rule out pityriasis rosea, and we must differentiate between dermatitis due to treatment with gold preparations and lupus erythematosus. In addition to the groups of follicular papules, there are areas in which the follicular papules have coalesced, forming scaly, crusted and exudative patches. I should say that this is a case of dermatitis due to treatment with gold preparations.

DR. LOUIS B. MOUNT: Though the eruption may be due to gold, I have never seen follicular lesions caused by a heavy metal with keratosis as marked as this man shows.

DR. LUDWIG OULMANN: My opinion is that we are dealing with a dermatitis caused by medication with a gold compound.

DR. ANDREW J. GILMOUR: It is impossible to make a clinical diagnosis on the first examination. This man had no follicular plugs until nine or ten days ago. He has a rather acute condition. I presented him for a diagnosis, and believed that possibly he had an eruption caused by medication with a gold compound.

ELEPHANTIASIS OF THE LOWER LIP. Presented by DR. MIHRAN B. PAROUNAGIAN.

Mr. T. K., aged 45, about eight months ago noticed a painless swelling of the lower lip. This swelling came on spontaneously and gradually disappeared. It recurred about five months ago and has persisted. There has been noticed, too, a gradual loosening of the front teeth in the lower jaw.

The patient stated that in 1917 he had a genital sore for which he treated himself. He underwent neither Wassermann tests nor treatment for syphilis.

The lower lip is diffusely enlarged to about four times its normal size; at its center it shows a vertical cleft. On the inner mucosal aspect are areas of leukoplakia, and there are similar lesions on the tongue; in one place there is a small superficial ulceration.

On April 3, 1933, the reaction to the Wassermann test was four plus.

DISCUSSION

DR. GEORGE M. MACKEE: I suggest treatment with vaccines, roentgen therapy and, perhaps, bacteriophage.

DR. FRED WISE: In my opinion the swelling is a chronic lymph stasis of the lip due to syphilis, and I suggest active antisyphilitic treatment.

RECKLINGHAUSEN'S DISEASE WITH LESION ON THE TONGUE. Presented by DR. MIHRAN B. PAROUNAGIAN.

E. A., a man, aged 28, for seven years had noticed the gradual appearance of swellings of various sizes on the forehead, face, neck, extremities and trunk. They were persistent and painless and ranged in size from that of a pinhead to that of a hazelnut. They were usually the color of the skin, but some had a darker, almost violaceous hue. Some were embedded in the cutis, merely raising the latter as a small swelling; others were inclined to be pendulous. The swellings were definitely nontender.

Examination of the oral cavity disclosed a rather large, irregular gyriform mass involving the left border and the undersurface of the tongue, also extending to the floor of the mouth. While the lesion was not painful, its size caused the patient to complain of discomfort.

I have not noticed similar lesions in cases of this type; that is why I presented this patient.

DISCUSSION

DR. DAVID L. SATENSTEIN: A clinical evaluation of the lesion on the tongue is possible only after a microscopic study of the tissue.

DR. HOWARD FOX: Considering the fact that the soft mass on the tongue occurs in a patient with typical Recklinghausen's disease, the probability is that the lesion is part of this disease, perhaps composed of fibrous or myxomatous tissue. I do not think that the unilateral distribution would in any way lessen the probability of Recklinghausen's disease.

DR. J. FRANK FRASER: I agree with the views of Dr. Parounagian.

DR. FRED WISE: In all probability, it is a lesion of Recklinghausen's disease. I do not believe that unilaterality is a point against such a diagnosis.

RUPIAL SYPHILIS, RECALCITRANT TO TREATMENT. Presented by DR. MIHRAN B. PAROUNAGIAN.

A man, aged 31, was first admitted to the clinic for diseases of the skin of the Bellevue Hospital, on Feb. 9, 1928. He then had a chancre of the sulcus (left), of four days' duration. The reaction to the Wassermann test was negative; the dark-field examination gave positive results. Treatment was instituted immediately; it consisted of eight injections of neoarsphenamine and fifteen of mercuric salicylate from February 9 to May 15. On June 26, the reaction to the Wassermann test was negative.

Further treatment consisted of six injections of silver arsphenamine and fifteen of mercuric salicylate, from July 3 to October 16. Wassermann tests made on Nov. 27, 1928, Jan. 15, March 7 and March 26, 1929 (spinal), Jan. 26 and March 2, 1931, and March 7, 1932, were negative.

On March 7, 1932, the patient presented a lesion on the prepuce of seven days' duration, following exposure three weeks previously. The dark-field examination gave negative results. The reactions to the Wassermann tests made on March 14, 18, 1932, were four plus. On March 23, 1932, the Wassermann test of the spinal fluid was negative.

Treatment was resumed. Eight injections of neoarsphenamine and twelve of mercuric salicylate were administered. On July 11, 1932, the reaction to the Wassermann test was four plus. A second course was started on July 18, and after five injections of neoarsphenamine and five of mercuric salicylate, dermatitis developed for which the patient was given a number of injections of sodium thiosulphate intravenously.

After he had recovered from the dermatitis, he was given a number of injections of thiobismol, sodium iodide, gold sodium thiosulphate and liver extract and mixed treatment with iron tonic. During the greater part of this period new tertiary manifestations developed on various parts of the body. The blood count was normal, and examinations of the urine did not reveal marked abnormality.

Silver arsphenamine was then given cautiously, and was followed by some improvement. In spite of all this, the patient still presented a number of rupial lesions which were most pronounced on the face.

DISCUSSION

DR. J. FRANK FRASER: My first impression was that this was an eruption caused by iodide or bromide. I should suggest injections of sodium chloride.

DR. HOWARD FOX: While a few of the lesions suggest iododerma, others are of the type seen in the late secondary or early tertiary period of syphilis. In my opinion the entire eruption is syphilitic.

ATROPHIA CUTIS MACULOSA. Presented by DR. MIHRAN B. PAROUNAGIAN.

C. A., a man, aged 21, had been admitted to the clinic for diseases of the skin of the Bellevue Hospital on March 10, 1933, with the following history. In the winter of 1929, a sore developed on the penis about six or seven weeks after exposure. He received local treatment only. About three months later he noticed the development of pinkish nodules of various sizes on the trunk, upper extremities and forehead, and a very few on the legs. These lesions did not itch or pain, but they continued to grow larger. Thereupon he consulted a physician.

After an examination of the blood, a diagnosis of syphilis was made. In the following three years, the patient received eighty-four injections into the arm and sixteen into the hip; the last treatment was received four months ago. While he was under treatment, the lesions became lighter and smaller; many disappeared completely.

The lesions on the back and on the abdomen are numerous and consist of small flat elevations, varying in size from that of a pinhead to that of a dime. They are inclined to be oval or fusiform in outline, about the color of normal skin and are firm to the touch. They are insensitive and show no inflammation. Interspersed here and there, especially on the anterior aspects of the chest and forearms, are a few areas of chalk-white skin, which, the patient claims, are the sites of previous lesions.

On March 10, 1933, the reaction to the Wassermann test was negative, and a blood count was normal.

DISCUSSION

DR. LOUIS B. MOUNT: I thought that some of the lesions resembled the tumor-like new growths of Schweninger-Buzzi.

DR. LUDWIG OULMANN: Even in the dermatosis of Schweninger-Buzzi, there is the question of primary or secondary atrophy, which can be decided only by careful microscopic examination.

DR. GEORGE M. MACKEE: I believe that this is an early case of macular atrophy. It is now in the edematous stage. Later, when there is degeneration of elastic tissue and degeneration or sclerosis of collagen, the atrophy may become conspicuous.

DR. HOWARD FOX: I entirely agree with the diagnosis of macular atrophy. The lesions are distinctly atrophic; they are not firm tumors. On palpation some of them give the sensation of possible invagination.

DR. FRED WISE: I agree with Dr. Parounagian. The condition is almost an exact replica of the cases described and illustrated by Darier in his textbook.

ARSENICAL DERMATITIS (LICHENOID TYPE). Presented by DR. MIHRAN B. PAROUNAGIAN.

A man, aged 41, contracted a sore throat after sexual exposure about six months ago. A physician, after making an examination of the blood, gave him a series of eleven intravenous injections of arsphenamine and nine of mercury.

The last injection of arsphenamine was given in January, 1933, about which time the patient first noticed the appearance of a rash on his body. This rash itched considerably at first. The eruption is extensive; it covers all the body excepting the face and neck. The lesions consist of large papules, covered with thin dry deep brownish scales, somewhat resembling psoriasis. There is a moderate alopecia, with slight leukoplakia on the buccal mucosa. A few lichenoid lesions are noted on the penis. On the palms and soles are discrete areas of keratosis which are suggestive of an arsenical origin.

The reaction to the Wassermann test made on March 22, 1933, was negative. The urine showed a faint trace of albumin and a few white blood cells. A specimen of urine was sent to our laboratory for examination for arsenic, but no report has been received.

The treatment has consisted of three intravenous injections of gold sodium thiosulphate.

DISCUSSION

DR. HOWARD FOX: I agree with the diagnosis, but I consider the clinical picture rather unusual.

LOS ANGELES DERMATOLOGICAL SOCIETY

NELSON PAUL ANDERSON, M.D., *Secretary*

Regular Monthly Meeting, Nov. 14, 1933

STANLEY O. CHAMBERS, M.D., *in the Chair*

ADENOMA SEBACEUM WITH TUBEROUS SCLEROSIS. Presented by DR. NELSON PAUL ANDERSON.

This girl, aged 16½, was first seen on Oct. 18, 1933, because of an eruption on her face which has been present all her life. She has also had firm hard masses projecting from the finger-nails and toe-nails for a number of years.

The history reveals that the mother died at the patient's birth and that the father died when she was 3 years old. Her stepmother, who has had the child only since the last of June, 1933, states that she is finding it hard to keep up her studies at school and also that her memory is poor and that her ability to think and reason is not the best.

There are typical shiny erythematous papules varying in size from that of a small split pea to that of a pinhead scattered over the face, particularly in the nasolabial folds and the central portion of the chin. In the center of the right cheek is a moderate-sized "port wine" mark.

To the right of the spine in the midlumbar region is a palm-sized area of skin in which all the follicles present a peculiar dimpled appearance. On the right index finger there is a firm, fibromatous, pea-sized lesion projecting from the base of the nail. The nail along the involved side is definitely depressed. There are no signs of the café-au-lait patches of abortive von Recklinghausen's disease. The index and middle fingers of the left hand are deformed and present lateral bowing. Roentgen examination of the fingers reveals an unequal growth of bone involving both the inner and outer sides of the phalanges.

DISCUSSION

DR. H. P. JACOBSON: This is an interesting case. The eruption is characteristic, and the individual elements are well defined. I am interested, however, to learn if possible, the nature of the lesion situated on the right side of the back. I shall appreciate it if the presenter will state how he classifies that lesion.

DR. NELSON PAUL ANDERSON: The patient has had no treatment. The case is interesting because of the congenital anomalies that the patient presents. The lesion on the back is difficult to classify. In New York I have seen similar lesions classified as dermatolysis. The lesion is as pronounced as it was when I first saw it.

(Drs. Wilhelm, Campbell and Goeckerman agreed with the diagnosis of adenoma sebaceum.)

LICHEN PLANUS OBTUSUS. Presented by DR. H. S. CAMPBELL.

Mrs. D. was first seen on Oct. 17, 1933, complaining of lesions on the trunk, head and extremities of about twelve months' duration. The first lesion appeared on the forehead. The lesions on the trunk appeared about four months ago. There is now a large serpiginous, papular, pigmentary lesion on the left side of the forehead. Scattered over the body are four or five lesions suggestive of psoriatic papules which contain whitish striae. Several rounded, whitish lesions are present on the tongue, and there are many arborescent, whitish striae over the mucosal surface of the vagina.

DISCUSSION

DR. SAMUEL AYRES JR.: I should not have thought of lichen planus from the lesion on the forehead. There is no question that the patient has lichen planus. All stages of transition can be seen between typical and extremely atypical lesions. I am not sure whether I should give the eruption the name of lichen planus obtusus. It is certainly an atypical type. My conception of lichen planus obtusus is of more hypertrophic, corneous lesions, such as are present on the legs.

DR. KENDAL FROST: When I first saw the patient the feature that suggested a diagnosis of lichen planus was the lesions on the tongue. The lesion on the forehead was suggestive of both lupus erythematosus and a rather superficial circinate syphilid. The patient may have more than one disorder.

DR. WILLIAM GOECKERMAN: From the appearance tonight, I could not make a diagnosis of lichen planus. Has a biopsy specimen been taken, and if not, could one be taken?

DR. L. F. X WILHELM: I saw several lesions of the type of lichen planus, but the picture as a whole is certainly not typical of lichen planus. I also should like to have a biopsy made.

DR. I. R. BANCROFT: The eruption resembles lichen atrophicus in some ways.

DR. C. R. HALLORAN: The lesions on the arms and in the mouth are those of lichen planus; however, the lesion on the forehead warrants the consideration of a serpiginous type of epithelioma. I should like to have a biopsy made on the lesion on the forehead.

DR. MOSES SCHOLTZ: I should not call the condition lichen planus obtusus, which presents a well defined clinical picture. It is, as a rule, nodular and is called at times prurigo nodularis. The patch on the forehead is distinctly atrophic. The lesion on the forearm looks like lichen planus. The locations are unusual for lichen of any type. It is hard to accept the diagnosis unless it is confirmed histopathologically.

DR. H. S. CAMPBELL: In his recent textbook Ormsby stated that the lesions of lichen planus obtusus may be flat or slightly convex, varying in size from that of a pea to that of a bean or larger. They are not always markedly hypertrophic. They may be situated anywhere. In this instance the only lesion complained of by the patient is the large one situated on the forehead, and this has apparently been traumatized. It is pigmented, manifests chronicity and has a decidedly suspicious outline. As the findings on examination of this lesion did not warrant a diagnosis, I made a general examination and discovered the other lesions. The two lesions on the back are somewhat suggestive of psoriasis. The raised, rounded

lesion on the wrist is distinctly a lichen planus papule, as is the one on the shoulder. The lesions on the tongue are distinctly lichen. However, I shall attempt to obtain a biopsy specimen.

LEPROSY. Presented by DR. STANLEY O. CHAMBERS.

This white man, aged 59, an American of Dutch extraction, has lived in the Philippine Islands for the past thirty-four years and is married to a native woman. For the past seventeen years he has had progressive atrophy, weakness and anesthesia of the hands and feet, the first symptom of which was numbness of the little finger of the left hand. About one year prior to the advent of numbness a macular, pinpoint erythematous eruption developed on the arms and back. The lesions gradually coalesced, and the involved areas became anesthetic. About one year after the development of anesthesia in the left hand, the right hand became involved. Four or five years later atrophy of the muscles of the hands and contracture of the fingers developed. A short time later the feet became similarly involved.

There is now a plaquelike, erythematous, infiltrated eruption over the trunk and extremities. The face and neck are relatively free. The primary lesion appears to be a small papule, which tends to coalesce. There is anesthesia of the upper extremities extending on the left to the shoulder and on the right to the elbow. Both lower extremities and the back below the midscapular region are likewise involved. There is atrophy of the entire tibial group of muscles with drop foot on one side and slight contracture of the toes. There is atrophy of all the small muscles of both hands, with contracture, producing typical claw hand. The Wassermann reaction of the blood was negative on Oct. 10, 1933. A nasal smear for Hansen's bacilli was positive on November 3. Biopsy showed a few Hansen bacilli present throughout the lesion examined.

DISCUSSION

DR. H. P. JACOBSON: This case of leprosy is of special interest and calls to mind the case of anesthetic macular leprosy which I presented before the society last spring with a tentative diagnosis of lupus erythematosus. My associates and I searched numerous times for lepra bacilli in nasal smears, in sections of tissue from the cutaneous lesions and in sections of nerve tissue removed from the postauricular nerve, all with negative results. It will be recalled that several of the members, especially Dr. Goeckerman, suggested the diagnosis of leprosy; a clinical diagnosis of anesthetic macular leprosy was also made by Dr. Frederick Reiss, professor of dermatology and leprology at the University Medical School of Shanghai, China. These two cases of leprosy should certainly serve as excellent reminders of the protean character of leprosy and of the ability of the disease to mimic almost every cutaneous affection.

DR. H. S. CAMPBELL: In the Hawaiian Islands, I saw about two hundred cases of leprosy and visited the leper settlements almost daily. I also saw some cases in India and Morocco. I have never seen anything like the diffuse type of eruption that this patient has.

A CASE FOR DIAGNOSIS (SYRINGOCYSTADENOMA?). Presented by DR. H. C. L. LINDSAY.

B. D. is a Bulgarian girl aged 7 years. The mother states that cutaneous lesions were first noted when the patient was 7 months old. These lesions were symptomless, and a few of them became smaller. She presents numerous small pigmented nevoid growths which have a predilection for the flexures of the body, particularly the axillae. Numerous lesions are present on the neck and eyelids. A few lesions are present on the back, but mostly over the scapular regions. The case is interesting because of the amount of glossy black pigment in the lesions. Microscopically the growths somewhat resemble syringocystadenomas. The epi-

thelium lining them has not broken through the basilar layers, and the cells are well formed and took the dye evenly. The lesions, therefore, do not resemble malignant growths, although they may be classified among the nonmalignant epitheliomas.

DISCUSSION

DR. C. R. HALLORAN: I agree with the diagnosis of syringocystadenoma.

DR. KENDAL FROST: I am not accustomed to the association of this degree of pigmentation with syringocystadenoma.

DR. WILLIAM GOECKERMAN: The case is interesting, especially since Dr. Lindsay makes a diagnosis of syringocystadenoma. I have never seen a case of syringocystadenoma with such marked pigmentation; for that matter, I did not know that those lesions had a tendency to be pigmented. The nationality of the patient is probably a factor.

DR. SAMUEL AYRES JR.: I think that the case is one of multiple pigmented verrucae of the neck. I did not observe any sweat gland tumors. In a hurried glance, the slides looked like solid epithelial structures. There are some pedunculated lesions on the neck, upper parts of the arms, chest and axillae. The pigmentation may have been accentuated because of the dark skin. Some of the lesions are filiform.

DR. STANLEY O. CHAMBERS: I am unwilling to accept the diagnosis of syringocystadenoma.

DR. H. C. L. LINDSAY: I consider the condition a nonmalignant epitheliomatous growth, and I think that it is more closely related to syringocystadenoma than to any other type. I have never seen a case with as much pigmentation as this one shows. That is why I brought the patient here. The pigmentation may be due in part to her nationality.

DR. H. P. JACOBSON: I was rather surprised to hear that the microscopic diagnosis was syringocystadenoma. Clinically, one gains the impression that the lesions are pigmented nevi. It is obvious, of course, that from the therapeutic standpoint a differential diagnosis between the two conditions is essential, and if the ultimate diagnosis is pigmented nevi the advisability of active therapeutic intervention, in my opinion, is questionable.

DR. STANLEY O. CHAMBERS: Since the subject has been revived, the histologic picture of syringocystadenoma is definite and, to my mind, cannot lead to such diagnostic uncertainty.

NELSON PAUL ANDERSON, M.D., *Secretary*

Regular Monthly Meeting, Dec. 12, 1933

STANLEY O. CHAMBERS, M.D., *in the Chair*

A CASE FOR DIAGNOSIS. Presented by DR. NELSON PAUL ANDERSON.

This white girl, aged 16, has had an abnormal condition of the gums for about one year. She first came to the White Memorial Hospital on Nov. 14, 1933, and gave the following history. About one year ago she was told by a dentist that she had a disease of the gums. Over a period of several months she received seven intravenous injections of neoarsphenamine, having been told that the gingival condition was Vincent's angina. The gums were treated locally with neoarsphenamine in dextrose.

On examination the gums presented a thin pseudomembrane which one was able easily to lift up from the gum tissue and strip back to the buccal reflection.

Such a procedure disclosed on the labial and buccal aspects of the gums fiery red gingival tissue which bled easily. On the lingual aspect only the membrane formation was present. There was no odor such as one would expect if the condition were Vincent's angina. A smear revealed only a few fusiform bacilli and spirilla of Vincent. The blood count revealed 78 per cent hemoglobin, 4,380,000 red cells, 8,570 white cells and a color index of 0.91. The differential blood smear revealed 75 per cent polymorphonuclears, 20 per cent lymphocytes, 4 per cent large mononuclears and 1 per cent eosinophils. The Wassermann reaction was negative, and the urine was normal except for a trace of sugar. Physical examination otherwise gave negative results except for leukorrhea which had been present for about one year and some traumatic adhesions of the labia which followed an injury at 5 years of age.

Treatment has consisted in swabbing the gums with an iodine preparation, metaphen, 10 per cent silver nitrate, tincture of iodine and mercurochrome. This treatment was without benefit, as was also the use of a sodium perborate mouth wash.

The patient is presented for the dual purpose of securing a diagnosis and suggestions for treatment.

DISCUSSION

DR. SAMUEL AYRES JR.: From merely looking at the patient I think that the condition is Vincent's angina. It seems to be responding to treatment. I understood the patient to say that there has been a membrane on the gums at times.

DR. NELSON PAUL ANDERSON: This is a peculiar case. The girl has had the condition for about one year. With a forceps one can retract the epithelium from the lower tip of the gum, but there is no false membrane. Histologic examination of a section showed only squamous epithelium. There seems to be no adherence between the epithelium and the underlying gingival tissue. I do not feel that the condition is due to a mouth wash. All internal medication has been stopped. There is a definite pathologic process in this case. A slide shows a few spirilla of Vincent. No cultures have been made.

DR. C. R. HALLORAN: All that I noticed was the redness of the mucous membrane. I did not know the history of the ability to remove the mucous membrane.

DR. NELSON PAUL ANDERSON: Has any one seen a condition like this in which the overlying epithelium can be stripped back from the gum?

DR. SAMUEL AYRES JR.: The gum looks transparent.

DR. NELSON PAUL ANDERSON: Another section has been taken from the gum tissue itself. The usual overlying epithelium is absent except at the top of the section.

DR. STANLEY CHAMBERS: I was struck with the possibility of scurvy.

DR. H. S. CAMPBELL: The marked pigmentation and the lack of sponginess of the gums are not typical of scurvy as I saw it at sea sometimes. The pigmentation is rather interesting. Could it be due to a dye that the patient had been using?

RECKLINGHAUSEN'S DISEASE. Presented by DR. NELSON PAUL ANDERSON.

This Negro school boy, aged 16, was presented before the society about one and one-half years ago. He then presented multiple small and large nodules scattered over the body, especially the extremities. In addition, there were marked left dorsal lumbar scoliosis and large café-au-lait pigmented macules. Roentgenograms of the entire skeleton taken in October 1932 failed to reveal any bony changes such as have been described in connection with Recklinghausen's disease. When the patient first came under observation he was backward mentally and was not doing well in his school work. His mother felt it necessary to come with him to the clinic at all times. When first seen, cod liver oil with extract

of malt was prescribed. This was given more as a placebo than as a therapeutic measure. In the course of six months a few more nodules developed, and the child gained some weight. During the first few months of 1933, however, no new lesions appeared, and some of the older lesions disappeared and others became smaller. In addition, the patient's entire mental make-up changed. This was noted by the physicians in attendance, by his school teachers and by his parents. I do not wish to convey the impression that the therapy given had anything to do with the improvement, for I believe it to be more likely that certain endocrine changes occurring at this age were the cause of the improvement. The patient is presented together with photographs to show the striking retrogression of many of the neurofibromas. The case is unusual, moreover, because of the occurrence of Recklinghausen's disease in a full-blooded Negro.

DISCUSSION

DR. H. C. L. LINDSAY: I observed a case of Recklinghausen's disease which developed shortly after the patient was struck by a shell. That patient had also painful subcutaneous fatty tumors, epehlides and acromegaly. The case presented here is clinically one of the most characteristic that I have seen.

CHARCOT'S JOINT (THREE CASES). Presented by DR. STANLEY CHAMBERS.

CASE 1.—This patient has had swelling of the right knee since 1926. The Wassermann reaction of the spinal fluid was positive in 1928, and he has had considerable antisyphilitic therapy. There is no pain in the joint involved. He has an associated mal perforant on the plantar aspect of the right great toe. The Wassermann reaction of the blood was negative on July 6, 1933.

CASE 2.—This patient has had swelling of the right thigh and knee since about 1927. A diagnosis of cerebrospinal syphilis with a Charcot joint of the right knee was made in April 1932. The Wassermann reaction of the blood was negative at that time, and that of the spinal fluid was positive. The colloidal gold curve was 4455555554. The patient has had considerable treatment with both neoarsphenamine and bismuth, the last treatment being in May 1933. The right knee is about twice the size of the left, and there are increased mobility and fluctuation.

CASE 3.—This patient has had swelling of the right knee since Oct. 1, 1933. There have been weakness and increased mobility of the joint since November 1. There is no pain. He gives a history of a penile sore in 1907. In 1917 an ulcer developed on the plantar aspect of the left great toe, which was subsequently amputated. The Wassermann reaction of the blood was positive at that time, and he was treated for six months. In 1928, an ulcer developed at the site of the amputation of the toe. The Wassermann reaction of the blood was negative, but that of the spinal fluid was positive.

DISCUSSION

DR. STANLEY CHAMBERS: These cases were grouped with the idea of showing various developmental changes in cases of Charcot's joint. I thought them interesting from this standpoint.

DR. SAMUEL AYRES JR.: The cases are interesting because of the characteristic lack of tenderness and pain. Such extensive destruction with almost no pain certainly suggests nerve involvement. It is an interesting contrast to note the great amount of pain and disability from a relatively slight roughening of the articular surfaces in ordinary arthritis.

DR. H. S. CAMPBELL: A fact which is always rather remarkable is the infinitely slight response of bony lesions to antisyphilitic therapy as compared to the response in other tissues.

PROBABLE SYPHILITIC ERYTHEMA NODOSUM. Presented by DR. STANLEY CHAMBERS.

This patient has had a nodular eruption on both legs for about six weeks. There is no associated pain or constitutional reaction. There is no history of primary or secondary cutaneous lesions of syphilis. While in military service in Panama in 1930 the patient became nervous, and both the blood and the spinal fluid gave a positive Wassermann reaction. The colloidal gold curve of the spinal fluid was 3555443211. He was given twelve injections of a bismuth preparation and twelve injections of tryparsamide and was then transferred to the Walter Reed Hospital, where a diagnosis of dementia paralytica was made. He received malarial therapy, sixteen fever cycles being induced, as well as sixteen injections of a bismuth preparation and fifteen of tryparsamide. He has had no antisyphilitic treatment since 1930.

He now presents on both legs, on the calves in particular, painless purplish nodules which vary from 0.5 to 1.5 cm. in diameter. On the calves, the nodules have coalesced so as to form a deeply indurated mass measuring about 3 by 5 cm. The Wassermann reaction of the blood was negative on Aug. 2, 1933.

DISCUSSION

DR. W. H. GOECKERMAN: This patient has dementia paralytica and was given malarial therapy. The indurated areas on the legs are not particularly suggestive of erythema induratum. Thus the suspicion of a gummatous infiltration in the skin arises, an interesting side-light on the mechanism of malarial therapy. Patients with such lesions have done well, in my experience, both clinically and serologically.

DR. SAMUEL AYRES JR.: I should not classify the condition as erythema nodosum. It is not painful, and it is on the calves rather than on the shins. It should be classified as erythema induratum. Various types of bacterial allergy can produce both clinical pictures.

DR. STANLEY CHAMBERS: To clarify the situation, the difference between syphilitic erythema nodosum and true erythema nodosum is that in the former, as is seen in this case, the clinical symptoms and signs are subdued yet there is a nodose appearance of the skin. The nodules of true erythema nodosum do not break down.

DR. H. P. JACOBSON: I am not entirely convinced of the correctness of the diagnosis of nodular syphilis in this patient. I think that the question of tuberculosis should be given some consideration. The patient on close questioning divulged that he has lost a good deal of weight in the past few weeks, that he feels feverish and has night sweats and that he has been losing strength. In view of the fact that he has been under continuous antisyphilitic therapy and that in the course of the treatment the cutaneous lesions made their appearance, it seems reasonable to eliminate the possibility of a tuberculous etiology before making a definite diagnosis of syphilis.

DR. H. C. L. LINDSAY: There is no reason why a syphilitic patient cannot have erythema induratum. It is not necessary for the lesions of erythema induratum to be caused by syphilis. One often sees two diseases in the same patient.

DR. C. R. HALLORAN: I did not see any lesions on the back of the leg but merely the nodular ones on the shin. There is no involvement of the joints. I think that the condition may be syphilitic erythema nodosum.

DR. M. N. ROSENBERG, by invitation: In regard to the recent loss of weight and night sweats, it may be stated that the patient has acute gonorrhea, which may be responsible.

ACTINIC DERMATITIS WITH LESIONS RESEMBLING HYDROA AESTIVALE ON THE FACE AND PRURIGO AESTIVALE ON THE ARMS. Presented by DR. SAMUEL AYRES JR.

This white girl, aged 6 years, has had an eruption almost constantly for about two years. The lesions appeared first on the face. The maternal grand-

father had asthma. Otherwise there is no history of allergy. The patient has had occasional sore throat and earache. The glands of the neck have been enlarged for a number of years. She has had many "stomach aches." The bowels have moved about once a day. When 16 months old she had convulsions, and, according to the mother, she nearly died. She has also been troubled with cramps in her legs. For six months the patient has been given daily treatments with ultraviolet radiation, without benefit, by another physician. Spectroscopic examination of the urine failed to reveal hematoporphyrin. Three examinations of the stools showed the presence of Giardia and Endamoeba coli. The eruption is limited to the exposed areas, the face and the extensor surfaces of the arms. On the face the skin is red, and there are a number of herpes-like vesicles, especially about the lips. Elsewhere there are many excoriations and bloody crusts. On the extensor surfaces of the arms there are scattered excoriated papules and nodules the size of a pea and larger, some of them secondarily infected.

DISCUSSION

DR. SAMUEL AYRES JR.: The diagnosis in this case is actinic dermatitis with lesions suggesting hydroa aestivale of the face. In regard to the finding of Giardia in the intestinal tract, I was told by an internist that Giardia may have a pathogenic significance if it is found in the duodenum. I recall one case of prurigo nodularis with lesions similar to the ones on this girl's arms. Endamoeba councillmania was found in the stools, and the condition entirely cleared under treatment directed toward the amebiasis. There is probably an underlying toxic condition which has sensitized this patient's skin to light.

DR. C. R. HALLORAN: I believe that the condition is closely related to lupus erythematosus. One frequently sees lupus erythematosus precipitated by sunlight at sea level. It would be interesting to take a section from one of the lesions for microscopic study.

DR. H. C. L. LINDSAY: Tuberculosis, diabetes and certain types of fungi make persons photosensitive.

LUPUS ERYTHEMATOSUS IN A CHILD. Presented by DR. NELSON PAUL ANDERSON.

A. C., a Mexican school girl aged 8 years, was first seen on Jan. 6, 1933, with an eruption on the face, the arms and legs and the upper part of the chest of a year's duration. There was no history of an allergic disorder in the patient or in the family. At that time a diagnosis of probable allergic eczema was made, and the patient was placed on an elimination diet and given local therapy. She then disappeared from observation until October 3, at which time the skin condition was unimproved, and there were vesicular lesions on the nose and both cheeks. By November 10, the eruption presented many aspects of lupus erythematosus, and she was placed on bismuth therapy. She has had three injections of 2 grains (0.12 Gm.) bismuth salicylate and has shown considerable improvement.

She now presents on the face an erythematous raised, papular eruption which has the general distribution of lupus erythematosus. On the backs of the hands are large, irregular plaques half the size of a palm which present the characteristic stippled appearance of lupus erythematosus. The lesions on the forearms are fairly large nondescript excoriated papules. The case is presented mainly on account of the youth of the patient.

DISCUSSION

DR. H. C. L. LINDSAY: I think that this is the type of case in which a gold tribromide preparation by mouth is of benefit. Gold and sodium thiosulphate is rather a dangerous drug to give a child. I observed an adult with photosensitivity whom I treated with a gold tribromide preparation by mouth with good results. The patient went on a trip around the world and was exposed to the tropical sun without suffering from photosensitivity.

DR. SAMUEL AYRES JR.: I have not had an opportunity to examine the patient in good daylight, but from the examination tonight I think that one would have to consider a diagnosis of actinic dermatitis in this case, which looks similar to the other cases of that condition. There is also the suggestion of scratching, as though the lesions had itched, and there is a slight suggestion of moisture in the lesions on the face.

DR. P. K. ALLEN, San Diego: I am interested in this case because I recently saw two Mexican girls with photogenic eczema one of whom had lupus erythematosus similar to that presented by this child. I have seen many young Mexican people, some of whom are very dark-skinned, who presented marked photosensitivity.

DR. KENDAL FROST: The picture presented by the Mexican girls is suggestive of lupus erythematosus, yet there seems to be absence of some of the cardinal features. I have seen patients with a similar eruption which proved to be merely seborrheic dermatitis or seborrheic dermatitis associated with light sensitivity and allergy. It seems to me that a biopsy is in order. In the other case, the sensitivity to light can probably be determined by patch tests either with radiation from the quartz mercury vapor arc lamp or with sunlight.

LUPUS VULGARIS WITH TUBERCULOUS ADENITIS. Presented by DR. H. P. JACOBSON.

H. H., a white woman, aged 33, of Russian-Jewish stock, presents a lesion on the left side of the face of ten months' duration. It commenced with a small "blotch" and has gradually enlarged to its present size and assumed its present character. The lesion is a sharply marginated, deep, erythematous plaque with several fairly characteristic nodules on the upper and inner borders. Under diascopic pressure characteristic apple jelly nodules are in evidence. Of interest is the fact that the patient also has tuberculous adenitis on the right side of the neck. The latter condition is of several years' duration, and responded readily to proper treatment about two and a half years ago. About ten years ago I treated the daughter (about 3 years old) of the patient for scrofuloderm. Except for occasional gastro-intestinal complaints (which some one diagnosed as chronic appendicitis) and some lack of endurance, the patient presents no subjective symptoms. She does not cough, is not short of breath, does not perspire at night and has not been losing weight. Lately she called my attention to a tender nodule the size of a split pea on the inner aspect of the left leg in about the middle third. This nodule, the patient states, is of about two months' duration, and examination conveys the impression that it is intimately connected with the underlying periosteum. The overlying skin is not involved in the process.

DISCUSSION

DR. H. C. L. LINDSAY: I could not make a diagnosis of lupus vulgaris on the basis of what I saw. I have not seen a case of this type since I have been in Pasadena.

DR. SAMUEL AYRES JR.: It is extremely rare to find lupus vulgaris originating in this climate. This condition certainly gives the impression of definite nodules. I think that clinically it is extremely suggestive of lupus vulgaris.

DR. W. H. GOECKERMAN: I am willing to admit that the condition is lupus vulgaris, but I could not satisfy myself. In an artificial light I could not see any apple jelly nodules.

DR. CHARLES CASKEY: Seeing the case only once, it was my impression that the condition is lupus vulgaris.

DR. H. P. JACOBSON: I consider this case especially interesting as it is the first example of lupus vulgaris of local origin which I have seen in this city in an experience of sixteen or seventeen years. I have known the patient and her family for about twelve years, and I treated her daughter for scrofuloderm about

ten years ago. Several years ago I treated the patient for tuberculous adenitis of the cervical glands on the right side of the neck. Two months ago she again consulted me because of a recurrence of the cervical adenitis, associated with the cutaneous lesion on the left side of the face and a solitary nodule on the left leg. Examination of the cutaneous lesion on the face revealed the presence of characteristic apple jelly nodules. At present the patient is receiving intravenous injections of colloidal copper morrhuate and filtered irradiation of the glands and is apparently responding well.

DR. NELSON PAUL ANDERSON: I do not think that one should accept this diagnosis without microscopic examination of a section. In the first place, it is rare for lupus vulgaris to start at this age. The apple jelly nodule, after all, is only an objective finding. As for scarring, if this is a lupus vulgaris I suggest that at the time the biopsy specimen is taken the whole lesion be surgically excised. There is a nodular form of lupus erythematosus.

DR. H. P. JACOBSON: In view of the fact that the lesion seems fairly active, it appears to me somewhat inadvisable to take a biopsy specimen and run the risk of further activating the infection, which would probably cause an unsightly scar. The suggestion of lupus erythematosus as a diagnosis appears to me untenable because morphologically there is total absence of all the essential criteria necessary for making a clinical diagnosis of that condition, namely, scaling, superficial atrophy and patulous follicles.

DETROIT DERMATOLOGICAL SOCIETY

WILLIAM G. SAUNDERS, M.D., *Secretary*

Regular Meeting, Nov. 28, 1933

HARTHER L. KEIM, M.D., *Presiding*

EPIDERMOLYSIS BULLOSA (?) IN BROTHERS. Presented by DR. WILLIAM G. WANDER.

J. K., aged 12, and B. K., aged 15, white boys, Polish, have been extremely liable to injuries since birth, and the wounds have healed only after long periods and with marked scarring. The father and an older sister are said to have a similar condition to a lesser degree. Epithelial proliferation is extremely slow, requiring three months for a lesion ½ inch (1.2 cm.) in diameter.

There have been no bullae, nor has there been any involvement of the mucous membranes, hair or nails. None of the lesions has appeared spontaneously.

There are many scars of various shapes and sizes, especially on the forearms and legs. The scars do not occur on the bony prominences particularly. They are sharply marginated, depressed, thin, pliable, smooth, dry and glistening. In general, the skin appears dry, smooth and pale, presenting an unctuous, velvety sensation to the touch.

Biopsy showed absence of glandular structure and hair follicles. There was a lack of white fibrous and connective tissue but an excess of elastic tissue.

DISCUSSION

DR. HOWARD J. PARKHURST: This interesting and peculiar familial skin defect does not present the typical picture of epidermolysis bullosa. These cases deserve further study.

DR. ARTHUR E. SCHILLER: I cannot consider the condition epidermolysis bullosa. The lack of bullae and of involvement of the mucous membranes and nails and the fact that the lesions do not appear spontaneously seem to point

against that diagnosis. The excess of elastic tissue also would be unusual. My opinion is that the condition is an ectodermal defect.

DR. WILLIAM G. WANDER: While these cases have much in common with epidermolysis bullosa, they do not conform in all respects with that disease. There have never been any bullae, nor have any of the lesions appeared spontaneously. Physical, laboratory and serologic examinations have disclosed no abnormalities.

Biopsy showed a thin layer of stratified squamous epithelium, regular in arrangement, with an average depth of about four cells.

The subcutaneous tissue is free from glands and hair follicles. There is a lack of connective and white fibrous tissue with a relatively marked increase of elastic tissue.

RAYNAUD'S DISEASE WITH CALCAREOUS DEPOSITS. Presented by DR. GEORGE VAN RHEE.

S. W., a white woman aged 20, single, American, presents lesions on the left elbow which appeared twelve years ago following an injury and some on the left knee which followed an injury ten years ago. There are also lesions on the right hand which began about ten years ago; there is no history of injury, but they are affected by cold.

The lesions on the left knee and elbow and on the terminal phalanges of the thumb and the index and middle fingers of the right hand are plaquelike. The plaques are studded with whitish-blue and yellow nodules the size of a pea. Some of the nodules are inflamed and slightly tender and seem to have undergone necrosis. The nodules on the fingers and thumb feel boardlike and atrophic and are slightly tender; they resemble sclerodactylia.

The blood count was normal. The blood sugar was 100 mg. per hundred cubic centimeters; the blood cholesterol, 158 mg. The Wassermann test of the blood was negative. Roentgenograms showed calcareous deposits.

Dr. S. W. Becker examined and reported on a biopsy specimen from the left knee as follows: "The epidermis is markedly thickened over the center of the section, and there is a suggestion of an opening extending part way through the epidermis, as though it may have been the opening of a sebaceous cyst. The material was decalcified a little too long to retain the basophilic properties of the calcium, and when it was received I noticed that the lower surface of the tissue showed considerable loose material which suggested a cystic content. There is no bone formation in this material, although I am sure that there was bone formation in the section sent me before. I therefore make a diagnosis of dermal calcinosis with a suggestion that the process may have taken place in an epidermoid or sebaceous cyst, although there is little evidence of a cyst wall. The condition does not appear to be calcified scleroderma."

DISCUSSION

DR. L. W. SHAFFER: This is an unusual case and worthy of further study in relation to calcification of the skin. I suggest general roentgen studies of the skeletal system for evidence of decalcification of the bones. The lesions, particularly at the tips of the fingers, could hardly begin as sebaceous cysts. Aside from the fact that such areas of calcification have been reported in Raynaud's disease, there is little to suggest this diagnosis.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. ROBERT C. JAMIESON and DR. G. WARREN HYDE.

M. S., a school girl aged 15, American, first noted a small erythematous lesion on the left cheek about five months ago. This became larger, and other lesions appeared on the cheeks and nose during the following three months.

When the patient was first seen, on Nov. 2, 1933, the lesions on the nose and cheek were of the typical "butterfly" type. On the forehead, neck, lips, mouth,

hands and arms were numbers of small, irregular erythematous lesions, some resembling toxic lesions, others of the lupus erythematous type. A few of these had begun as vesicles. The lips were swollen and fissured, and the palate was studded with small erosions with bright red areolae. The temperature was 102 F.; the pulse rate, 124.

According to the history the patient received two intravenous injections of gold sodium thiosulphate, 50 mg. each, and one of a bismuth compound, after which she became rapidly worse.

During hospitalization, from November 4 to November 20, she improved rapidly, and on discharge the toxic lesions had practically disappeared, leaving some pigmentation. The original area of involvement over the nose and cheeks had involuted almost completely.

The leukocyte count on November 4 was 5,700; on November 10, 3,500, and on November 17, 10,500.

The Pirquet test was negative. Roentgen examination of the chest revealed nothing abnormal.

NECROBIOSIS LIPOIDICA DIABETICORUM (URBACH). Presented by DR. HAROLD TONNENHOLZ (by invitation).

This Jewish girl, aged 19, single, has two lesions on the anterior portion of the lower third of each leg. The first lesion began three years ago on the left leg. It enlarged gradually to the size of a nickel, and others developed. The lesions are lividly erythematous, slightly raised, sharply demarcated, circular and oval nodules 1 cm. in diameter, coursed by telangiectatic vessels at the border and covered with rather thin, closely adherent scales. The center of the oldest lesion is hard, flat and atrophic, with a slightly yellowish color surrounded by a bluish-violet border. They are firm but not tender and under pressure appear yellowish. The patient has had mild diabetes for five years.

The blood sugar has varied from 174 to 286 mg. per hundred cubic centimeters. The urine has remained sugar-free. The blood cholesterol on Nov. 20, 1933, was 129.5 mg. per hundred cubic centimeters.

This case was presented before the Detroit Dermatological Society by Dr. William G. Saunders, on Feb. 10, 1933, as one of sarcoid (?).

Biopsy showed the structure of necrobiosis lipoidica diabeticorum.

DISCUSSION

DR. HOWARD J. PARKHURST: This case seems to be similar to the more extensive one which was presented in June 1933 by Dr. Zeisler at the meeting of the American Dermatological Association in Chicago.

DR. LOREN W. SHAFFER: The condition, I believe, is a typical example of the new diabetic metabolic dermatosis recently described in the German literature by both Oppenheim and Urbach. The histologic picture and the clinical findings are typical, as compared with Urbach's detailed description. An example of this condition was presented in Chicago in June 1933, at the clinic for the American Dermatological Association.

PARAPSORIASIS (?). Presented by DR. CYRIL K. VALADE.

This school boy, aged 15, American, states that a patch of dermatitis the size of a dollar appeared eight months ago on his right leg. The patch increased in size, and others formed, spreading to both arms and both legs. They are erythematous, scaly areas with associated papules. The borders are definite and slightly infiltrated. There are cracking and scaliness between the toes.

No laboratory studies have been made.

DISCUSSION

DR. HOWARD J. PARKHURST: These lesions may be dermatophytids resulting from infection of the feet.

TRICHOPHYTOSIS (?) OR TRICHOPHYTID (?). Presented by DR. LOREN W. SHAFFER.

This white girl, aged 20 months, has an eruption which began on the feet four months ago. The whole plantar surface, including that of the toes, was involved. It was vesicular, erythematous and fairly sharply defined, the lesions drying to crusts and desquamating in tenacious shreds.

Shortly after the onset of the disturbance sharply defined, coin-sized patches of dermatitis appeared rather profusely on the arms and legs, with scattered lesions on the trunk and face. The patches are edematous and slightly raised, with a suggestion of infiltration and depth on palpation. The older lesions are covered with a fine tenacious scale.

There is no history of the administration of drugs or laxatives.

Two examinations for fungi revealed only a single suggestive mycelial thread. A Wassermann test has not been made.

Treatment for the past month with local applications, directed toward the relief of epidermophytosis or trichophytid, has caused but slight improvement.

DISCUSSION

DR. LOREN W. SHAFFER: There is a suggestion of psoriasis in this case. Further observation will be necessary to establish a diagnosis.

LICHEN PLANUS, GENERALIZED AND HYPERTROPHIC. Presented by DR. WILLIAM G. WANDER.

J. C., an Italian school boy, aged 14, has an itchy scaly eruption of seven years' duration on the right tibia, which was originally diagnosed as psoriasis.

Six weeks ago a generalized eruption appeared, which has persisted without modification. It covers the entire body except the face, hands and feet. The lesions are large papules, red and violaceous, with some scale.

There are lesions on the right buccal mucosa. The lesions on the right tibia are scaly, piled up and confluent, extending in a patch about 2 by 6 inches (5 by 15 cm.) over the middle third.

There is intense itching, especially about the genitalia and the cubital fossae.

DISCUSSION

DR. WILLIAM G. WANDER: The question of diagnosis is not open in this case. The condition is frankly lichen planus. The boy has been asked to come here because of the generalization of the eruption and his age. The scaly eruption on the right leg is hypertrophic lichen planus and I think was of the same type seven years ago. That such an eruption should persist for seven years and then suddenly become generalized is of more than ordinary interest.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

EUGENE F. TRAUB, M.D., *Secretary*

Regular Meeting, Dec. 5, 1933

LEO SPIEGEL, M.D., *Chairman*

CARCINOMA (?). Presented by DR. DAVID BLOOM for DR. C. H. MARTIN.

This white man, aged 49, born in the United States, presents on the glans penis a firm, whitish, warty lesion which extends into the meatus. It started

eight months ago with a small warty lesion near the meatus and spread until it involved the whole glans penis, destroying it partly. In the right groin there are firm glands the size of a hazelnut. In order to study the whole lesion, the prepuce has been split dorsally. Histologically the lesion was reported by Dr. Riordan to be a granuloma.

DISCUSSION

DR. J. FRANK FRASER: On clinical grounds, my diagnosis is carcinoma. Another biopsy should be made.

DR. GEORGE C. ANDREWS: The condition is characteristic of papillary carcinoma of the glans penis. The age of the patient, the firmness of the lesion, the elevated border, the papillary appearance and the enlarged inguinal glands point to that diagnosis.

DR. ISIDORE ROSEN: It would be advisable to rule out syphilis before undertaking any radical treatment. I have seen ulcerations of this type due to tertiary syphilis, and I should consider this diagnosis, especially in view of the fact that the pathologic report was granuloma.

DR. WILLIAM CURTH: I have seen a couple of such cases in Buschke's clinic in Berlin (described by Loewenstein: *Klin. Wchnschr.* **4**:1726, 1925) which were caused by venereal warts. Infiltrating venereal warts sometimes become malignant. They are infiltrating on account of the mechanical condition caused by phimosis.

DR. T. J. RIORDAN: We made two biopsies, and both showed nonsyphilitic granuloma. We thought that we did not get enough material, and another biopsy was requested.

DR. HERMANN FEIT: When one sees venereal warts in men past the age of 40, the possibility of carcinoma must always be taken into consideration.

DR. WALTER JAMES HIGHMAN: There are five or six diagnoses that any dermatologist would think of in this case. The correct one must be determined by histologic study and specific therapy. According to Dr. Fraser, the lesion looks like carcinoma of the penis. The only thing that I disagree with in the presenter's diagnosis is the question mark.

DR. DAVID BLOOM: The Wassermann test of the blood was negative, and no history of syphilis could be elicited. Phimosis developed, as far as I could ascertain, after the development of the tumor. I therefore assume that the tumor was not produced by the phimosis. In spite of the probable clinical diagnosis of a malignant growth, the question mark after the diagnosis is justified, for the histologic report on two biopsy specimens was granuloma. Further biopsies will be made to ascertain the exact diagnosis.

KELOID (?). Presented by DR. GEORGE C. ANDREWS.

This woman, aged 35, born in Russia, noted a "pimple" on her chest about ten years ago. There was no history of injury preceding this. The lesion has gradually increased in size, rather rapidly during the last few months. She has received no therapy except home remedies. The lesion is red and glistening and measures 4.5 by 3 cm. in diameter. It is situated approximately 1 inch (2.5 cm.) below the midportion of the left clavicle. It is firm, nonfluctuating and nontender.

Biopsy showed moderate edema of the epidermis and corium. About the blood vessels of the corium was a moderate infiltration of mononuclear cells. A few of these cells were lymphocytes, but most of them were spindle cells. A few polymorphonuclears were also seen. Fibrosis had occurred about the sebaceous glands. No histologic diagnosis was made.

DISCUSSION

DR. MAX SCHEER: I examined the lesion before reading the histologic report, and my impression was that it was a sarcoid. I suggest that another biopsy be made.

DR. WALTER JAMES HIGHMAN: I venture to say that a more careful inspection than is afforded as a rule at meetings would support my impression that this dusky red lesion, which is as hard as a rock, discoid and set deep in the skin, is early scleroderma. The histologic observations support this belief. The cuff or scabbard of a nondescript round cell deposit surrounding the vessels and the edema of the connective tissue further support this view.

DR. GEORGE C. ANDREWS: This case is presented as one of keloid with a question mark. One biopsy has been made, but the results were far from satisfactory. The section was taken fairly far from the center of the lesion. Another biopsy will be made, and the case will be presented again.

BOWEN'S PRECANCEROUS DERMATOSIS. Presented by DR. GEORGE C. ANDREWS.

E. Z., a woman aged 68, single, gives a history of a small warty growth which has gradually increased in size. The lesion has been present for five years. It is located on the dorsum of the right index finger near its base, extending into the web, and is sharply demarcated, erythematous and somewhat infiltrated, with heavy crusting and fissuring. After removal of some crusts a reddish granulating surface is visible. On the dorsum of the hand is an erythematous scaly lesion the size of a bean, slightly raised with a sharply defined and somewhat rolled edge.

Biopsy showed a small piece of skin the pathologic structure of which presented many artefacts. Parakeratosis with vesicle formation was noted. Acanthosis was marked. Within the hypertrophied area were seen masses of swollen, clear cells with large vesicular nuclei. Multinucleated clumping forms were present. The penetrating epithelial pegs were well delimited by a basement membrane. Mitotic figures were discerned within the area of pathologic change. The corium was the site of a marked inflammatory reaction which was definitely chronic. A diagnosis of Bowen's precancerous dermatosis was made.

DISCUSSION

DR. GEORGE C. ANDREWS: In addition to the lesion described, there is a keratotic spot on the dorsum of the hand near the wrist. This thickly crusted lesion first gave me the impression of Bowen's disease. Histologic examination showed swollen, clear cells with large nuclei characteristic of Bowen's disease.

ULERYTHEMA OPHRYOGENES (?). Presented by DR. HERMANN FEIT.

R. B., a woman aged 41, for a year has had persistent erythema on the border of the hair line and over the preauricular region and scalp. These areas are edematous and covered with multiple follicular papules which have necrotic centers not unlike those seen in acne varioliformis. The hairs in these follicles are either broken off or absent. The entire involved area is indurated.

Biopsy showed edema but no other definite changes in the epidermis. The corium was also edematous and showed marked infiltrations of lymphocytes, arranged in large nodules. Such infiltrations were observed also in the hypoderm. They seemed to bear a relation to the blood vessels and hair follicles. A network of stellate cells was seen in the masses, and a few eosinophils were also noted. The sections were highly suggestive of lymphoblastoma.

DISCUSSION

DR. PAUL E. BECHET: I cannot agree with the diagnosis of ulerythema ophryogenes. All of the characteristic features of the disease are absent. There is no thinning of the hair of the eyebrows with subsequent superficial cicatrization, and the bearded region is unaffected. There is no erythema with elevated horny papules at the mouths of the hair follicles. The lesion strongly suggests acne varioliformis, and I regard that diagnosis as most probable.

DR. LOUIS TULIPAN: My impression of ulerythema ophryogenes has always been horny plugs in the hair follicles, especially of the eyebrows, with subsequent ulceration, atrophy and alopecia, which are not present in this case. My impression is that this is a fairly typical case of acne varioliformis.

DR. MARION B. SULZBERGER: I think that probably Dr. Feit means ulerythema sycosiforme. If so, I agree with the diagnosis. I could not find any atrophy of the eyebrows. This is practically constant in ulerythema ophryogenes, although of course ulerythema ophryogenes can affect other parts as well, for instance the sides of the scalp and the bearded area.

DR. HERMAN FEIT: One half of the right eyebrow is absent, and only follicular horny plugs are present. Darier pointed out the involvement of the preauricular area in ulerythema ophryogenes, and this area is affected in this case. Brocq tried to line up this condition with monilethrix. Stellwagon said that the disease sometimes resembles seborrheic dermatitis; at other times small horny projections are seen at the mouths of the follicles, or later follicular atrophy appears. In acne varioliformis one sees acne-like lesions on an erythematous base with deep-seated dry crusts or later pitted scars, and not erythema covering large areas with fine follicular keratoses. Lupoid sycosis is a peculiar type of sycosis vulgaris which heals with atrophy in the center. As the histologic picture suggests lymphoblastoma, I will try to obtain a specimen from a different part of the face.

A CASE FOR DIAGNOSIS (KERATOSIS PALMARIS ET PLANTARIS?). Presented by DR. LOUIS TULIPAN.

P. T., a white man aged 47, states that eleven years ago he had two lesions on the penis followed by a bubo, which was incised. He received only oral treatment until about one and a half years ago, when he learned that his wife and 6 year old son, who were in Italy, had positive Wassermann reactions of the blood. Although he had had a negative reaction, he received intramuscular injections of bismuth and neoarsphenamine. After six injections of neoarsphenamine, lesions developed on the palms, soles and penis. The lesions of the palms and soles, although improved while under treatment with sodium thiosulphate, never cleared completely. The penile lesion disappeared after six months only to recur four months ago. At the last examination the patient presented on the palms and soles irregular, keratotic patches with some fissuring. On the glans penis there was a superficial, irregular, ill-defined erythematous lesion with an adherent grayish-white scale and some fissuring. Several Wassermann tests of the blood have been negative.

DISCUSSION

DR. PAUL E. BECHET: I suggest that an arsenical test be made on the urine. The most probable diagnosis is arsenical dermatitis. The fact that the patient improved with sodium thiosulphate is also somewhat in favor of that diagnosis.

DR. WALTER JAMES HIGHMAN: Is it clearly established that this patient did not have any lesions on the palms and soles before he received arsenic?

DR. LOUIS TULIPAN: The keratotic lesions on the palms are such as may be seen in psoriasis. That diagnosis may be considered. Another suggestion is erythroplasia of the glans penis. That, however, does not explain the keratosis on the palms and soles. The third diagnosis to consider is arsenical keratosis. I will make a test for arsenic on the urine.

RESULTS OF INTRADERMAL TESTS WITH VARIOUS VACCINES, USING MEASURED AMOUNTS OF NITROGEN: PRELIMINARY REPORT OF EXPERIMENTAL WORK. Presented by DR. HERMAN GOODMAN.

CASE 1.—P. W., a white woman aged 56, was seen on Nov. 25, 1933, at which time she received test injections for tinea. She was examined again on November 28. The results obtained are shown in table 1 A.

The patient gives a history of having had typhoid thirty years ago. A macroscopic tube agglutination test of her serum gave results shown in table 1 B.

The microscopic examination for tinea was positive on November 28.

TABLE 1 A.—*Results of Test Injections in Case 1*

Material Injected Intradermally	Dose, Mg. of Nitrogen in Test Material	Result 11/28/33	Result 12/5/33
Outer Aspect of Right Forearm			
Trichophytin	0.0116	1 plus	Scaly
Staphylococcus-streptococcus vaccine	0.0112	1 plus	
Typhoid vaccine	0.0122	2 plus	Scaly
Gonococcus vaccine	0.0092	Negative	
Outer Aspect of Left Forearm			
Trichophytin	0.0120	2 plus	Scaly and itchy
Staphylococcus-streptococcus-colon bacillus vaccine	0.0112	1 plus	
Typhoid-paratyphoid vaccine	0.0112	3 plus	Scaly
Control, broth medium	0.010	Negative	

TABLE 1 B.—*Results of Macroscopic Tube Agglutination Test in Case 1*

Culture	Dilution 1:20	1:40	1:80	1:160	Negative Control
18 hour broth culture Bacillus typhosus (Mount Sinai)	4 plus	3 plus	3 plus	1 plus	Negative
Bacillus paratyphosus A	Negative	Negative	Negative	Negative	Negative
Bacillus paratyphosus B	Negative	Negative	Negative	Negative	Negative

CASE 2.—A white woman aged 42 reported to the clinic on Dec. 2, 1933, with a diagnosis of eczema. She received test injections for eczema in the left thigh on December 2 and was examined again on December 4. The results are shown in table 2.

CASE 3.—B. B., a white man aged 44, came to the clinic with a diagnosis of tinea in the groins. Test injections were begun on Dec. 2, 1933, and the patient was again examined on December 5. The results are shown in table 3.

DISCUSSION

DR. WALTER JAMES HIGHMAN: Had these patients previously had tinea?

DR. SAMUEL PECK: It is difficult to discuss Dr. Goodman's charts in detail because of their intricacy. Peculiarly, some of the charts which I studied gave me the impression that Dr. Goodman has proved the opposite of his thesis, namely, that irrespective of the amount of nitrogen the reaction depends more or less on the hypersensitivity of the patient, because in a number of instances a vaccine containing much less nitrogen than another gave a much greater reaction. I gather that Dr. Goodman is trying to deflate the value of a trichophytin reaction for the specificity of any intradermal test because of the great number of positive reactions which he obtained. This is important and emphasizes the necessity for experience in evaluating any cutaneous test. I am sorry that tuberculin was not included as one of the test substances, because I am sure that Dr. Goodman will agree that that produces a specific reaction. One must differentiate between a primary toxic substance and a primary reactivity of the skin in evaluating a cutaneous test. Experience shows that streptococcic vaccines usually give reactions. Whether this is due to a primary toxic substance or to a widespread hyper-

sensitivity is difficult to determine. A reaction due to hypersensitivity usually lasts much longer than the nonspecific reactions. The work of Bloch has shown that the specific substance in trichophytin on which the positive reaction rests is a polysaccharide and not a nitrogen-containing substance. I think that the material which Dr. Goodman has presented is not extensive enough to warrant

TABLE 2.—*Results of Test Injections in Case 2*

Material Injected Intradermally	Dose, Mg. of Nitrogen in Test Material	Result
Outer Aspect of Right Thigh		
Trichophytin	0.0116	Negative
Staphylococcus-streptococcus vaccine	0.0112	2 plus
Typhoid vaccine	0.0122	1 plus
Gonococcus vaccine	0.0092	1 plus
Inner Aspect of Right Thigh		
Trichophytin	0.0116	Negative
Trichophytin	0.0232	Negative
Trichophytin	0.0348	Negative
Inner Aspect of Left Thigh		
Trichophytin, special	0.0120	1 plus
Staphylococcus-streptococcus-colon bacillus vaccine	0.0112	1 plus
Typhoid-paratyphoid vaccine	0.0112	1 plus
Control, broth medium	0.010	Negative
Outer Aspect of Left Thigh		
Control, broth medium	0.010	Negative
Control, broth medium	0.020	Negative
Control, broth medium	0.030	Negative

TABLE 3.—*Results of Test Injections in Case 3*

Material Injected Intradermally	Dose, Mg. of Nitrogen in Test Material	Result
Outer Aspect of Right Forearm		
Trichophytin	0.0116	1 plus
Staphylococcus-streptococcus vaccine	0.0112	1 plus
Typhoid vaccine	0.0122	1 plus
Gonococcus vaccine	0.0092	1 plus
Inner Aspect of Right Forearm		
Trichophytin	0.0116	1 plus
Trichophytin	0.0232	1 plus
Trichophytin	0.0348	1 plus
Inner Aspect of Left Forearm		
Trichophytin, special	0.0120	1 plus
Staphylococcus-streptococcus-colon bacillus vaccine	0.0112	1 plus
Typhoid-paratyphoid vaccine	0.0112	1 plus
Control, broth medium	0.010	Negative
Outer Aspect of Left Forearm		
Control, broth medium	0.010	Negative
Control, broth medium	0.020	Negative
Control, broth medium	0.030	Negative
	(Showed some stain, no erythema and no infiltration)	

any definite conclusions. Certainly arguments of this kind do not speak against the fact that there exists a hypersensitivity to trichophytin.

DR. MARION B. SULZBERGER: I do not quite understand what Dr. Goodman is trying to prove in his demonstration tonight. It cannot be that he thinks that the specificity of the reaction to trichophytin is in any way invalidated by the fact that these patients also react to extracts of other micro-organisms, for every one knows that this is almost always the case. In general, a reaction of the skin to an extract of a micro-organism means merely that the person has had intimate

contact with the bacterium, bacillus or fungus or its relatives. Obviously, therefore, every one will react to extracts of many different strains—frequently, for instance, to streptococci, staphylococci, tubercle bacilli, epidermophyton (or trichophyton) and Monilia, for who has not had at some time contact or infection with these organisms?

I repeat, however, that this does not refute the statement that the trichophytin reaction is highly specific. Its specificity has been proved by over thirty years of assiduous researches, both on human beings and on animals, carried out by the schools of Jadassohn and Bloch and many others. When one speaks of the specificity of a cutaneous reaction one means that the reaction is positive only in those who have been sensitized by the organism in question or by one of its immediate relatives. Among the observations which prove this to be true in the case of Trichophyton and trichophytin are the following:

(*a*) Animals infected by fungi of the Trichophyton group give positive reactions; noninfected animals do not (B. Bloch and subsequently several hundred other investigators).

(*b*) In countries in which infections with the Trichophyton group in human beings are rare, positive reactions to trichophytin are rare. In countries, such as the United States, in which infections with Epidermophyton (which belongs to the same immunologic group as Trichophyton) are extremely frequent, positive reactions to trichophytin are also extremely frequent.

(*c*) In localities in which infections with Trichophyton are frequent the percentage of positive reactions increases with the ages of the groups of children tested; that is, it runs parallel and proportional to the opportunity for preceding infection (Rosen, Peck and Sobel).

(*d*) Prausnitz-Küstner antibodies (reagins) have been shown to exist which are specific for Trichophyton, reacting with fungi of this group and not reacting with Monilia and other fungi. (Experiments in Passive Transference of Urticarial Hypersensitiveness to Fungous Extracts, *J. Immunol.* **23**:73, 1932).

(*e*) The uterine strip of guinea-pigs infected with Trichophyton reacts with trichophytin and not with other extracts. The uterine strip of noninfected animals does not react. (Jadassohn, W.; Schaaf, F., and Sulzberger, M. B.: Der Schultz-Dalesche Versuch mit Trichophytin, *Klin. Wchnschr.* **11**:857, 1932).

There are, of course, innumerable other factors which practically prove the specificity of the trichophytin reaction, but which I cannot take the time to record here.

As to the question of the nitrogen content of trichophytin, I believe that the experiments of Bloch, Labouchère and Schaaf (*Arch. f. Dermat. u. Syph.* **148**:413, 1925) and those of Werner Jadassohn, Schaaf and myself, just cited, make it a probability approaching certainty that the reaction is dependent not on the nitrogen content of the extract, but on a starchlike, specific polysaccharide, which, however, may contain a little nitrogen. At any rate, I have always been able in testing trichophytin-hypersensitive skins, to elicit specific reactions of great intensity with a specific trichophytin polysaccharide containing practically no nitrogen and, as far as can be determined, no protein.

DR. SAMUEL PECK: I should like to recall to the section my experimental reproduction of hypersensitivity to trichophytin (Epidermophytosis of the Feet and Epidermophytids of the Hands, ARCH. DERMAT. & SYPH. **22**:40 [July] 1930). A girl with a negative reaction to trichophytin was infected with a pure culture of Epidermophyton Kaufmann-Wolf on the feet. The disease at its height resembled intertriginous mycosis of the feet. The lesions on the feet reached their acme in twenty-four days. Fungi could be demonstrated a week later. Thirteen days after the beginning of the experiment the trichophytin reaction became positive, and in the following weeks it became stronger. Twenty-four days after the beginning of the experiment a few dyshydrotic lesions appeared on the fingers of the right hand. A reinfection was produced on the feet of the patient after the original infection had subsided. The lesions reached their acme in six days

and were much more vesiculopustular than the previous ones. The trichophytin reaction was strongly positive. Two weeks after the beginning of the experiment there was a generalized dyshydrotic eruption on both hands. There is no question that in this case all the requirements were fulfilled for the experimental reproduction of a disease which depends on hypersensitivity to trichophytin.

DR. JESSE TOLMACH: The specificity of trichophytin is not regarded as absolute by all observers. It has been disputed by J. Jadassohn, Arnold, Sloimovici and Ullmo, Darier, and Ravaut. The trichophytin reaction is not infrequently negative in cases of dermatomycosis in which fungi are demonstrable in the feet and in which there are so-called epidermophytids of the hands. Traub and I reported such cases in a recent article (Epidermophytids and the Trichophytin Reaction, ARCH. DERMAT. & SYPH. **28**:560 [Oct.] 1933).

DR. LEWIS BYRNE ROBINSON: I admire Dr. Goodman for trying something. If he can produce five or six different reactions, it certainly is an accomplishment. I should like to know further why such reactions occur.

DR. WALTER JAMES HIGHMAN: I feel as Dr. Robinson does. I do not know much about the technicalities under discussion. I see theoretical objections to Dr. Goodman's work because most persons are sensitized to some or all of the organisms that he mentions. All dermatologists know that as a diagnostic aid the trichophytin test has little value in New York, but this does not affect its specificity. It merely indicates the frequency of tinea in this vicinity.

DR. MARION B. SULZBERGER: "Specificity of a reaction" means that the reaction is produced only by the same substance which has caused the sensitization or by one immunologically related to it. It does not mean that all persons who have been infected by an organism must acquire hypersensitivity to that organism. Nor does it mean that a reaction must be *diagnostic*. It must be apparent that even a highly *specific* reaction such as the cutaneous reaction to tuberculin or trichophytin is *not diagnostic* in a community in which practically all persons have had a prior infection with tubercle bacilli or Trichophyton. Whether the skin disease under investigation is a gumma, scabies, an occupational dermatosis, an artefact or frostbite, in New York the chances are at least eight in ten that the adult patient will have a positive trichophytin reaction. Its positivity is *specific*, for it means that that person has been infected by fungi of this group; it is *not diagnostic*, for it does not prove that the disease at the moment under investigation is due to fungi. Among others, Dr. Williams, Dr. Peck and I have during the last few years been trying to emphasize and plead for the recognition of this state of affairs, and it seems that we have not as yet been understood. My own findings and opinions on this subject have been set forth in numerous instances (*J. Allergy* **2**:11 [Nov.] 1930, footnote; *M. Clin. North America* **14**:1557 [May] 1931; *J. A. M. A.* **99**:1759 [Nov. 19] 1933; *Am. Med.* **28**:4 and 416 [June] 1933). Recently an article appeared in the ARCHIVES which again confused the issues of the *diagnostic* and *specific* qualities of the trichophytin reaction.

Even the most specific skin test cannot be 100 per cent accurate. As Dr. Robinson says, a certain percentage of persons infected with fungi of the Trichophyton group do not give a positive reaction to trichophytin. It is possible that in these persons the tested skin areas either have never become hypersensitive to trichophytin or, more likely, have become first hypersensitive and then immune, as Wise and I showed could be done artificially by repeated injections (Ringworm and Trichophytin, *J. A. M. A.* **99**:1759 [Nov. 19] 1932). Recently trichophytin-neutralizing antibodies (trichophytin anticutins) have been demonstrated in the blood stream of such patients. An abstract on this subject appeared in the Year Book of Dermatology and Syphilology for 1933 (Chicago Year Book Publishers, 1934).

DR. JESSE A. TOLMACH: A comparison of the reactions to tuberculin with those to trichophytin is not entirely proper. Tuberculosis is unquestionably a systemic disease. With the exception of a rare finding of fungi in the human

blood stream, superficial epidermophytosis has not been proved to be systemic. Complement-fixation tests in the latter condition are not conclusive.

DR. HERMAN GOODMAN: Three patients were exhibited who had had intradermal injections of trichophytin and staphylococcus, streptococcus, colon bacillus, typhoid, paratyphoid and gonococcus vaccines. The dose was determined by measuring the nitrogen in these materials and then injecting equivalent amounts of nitrogen. This procedure differs from the usual one, by which equivalent volumes of vaccine and trichophytin are injected intradermally. The unit of nitrogen was chosen because of its ease of determination and not because of any preconceived idea that the reaction excited was due to the nitrogen.

The results obtained on these three patients and those shown in the chart for ten patients not exhibited were interesting. A series of patients who gave no evidence of tinea microscopically or clinically gave positive reactions to trichophytin and positive skin reactions to intradermal injections of vaccine which were indistinguishable from the reaction to trichophytin. Some other patients gave negative reactions to trichophytin but positive reactions to other materials. One patient with a very strong reaction to typhoid vaccine was found to give a strongly positive Widal reaction. Other patients gave no reaction to any one of the vaccines injected. As a control, an equivalent amount of nitrogen in broth medium was injected. In no patient did this excite any local reaction. The matter is now under further consideration and will be offered for publication in the ARCHIVES.

DR. SAMUEL PECK: Usually in cases of hypersensitivity to trichophytin there is a group reaction; that is, a patient infected with one type of ringworm will show a reaction to an extract made from cases of other types. In the last case mentioned by Dr. Tolmach there is a possibility that there is a more specific hypersensitivity to trichophytin and that had a test been made with an extract of the organism causing the lesions the reaction would have been positive.

GRANULOMA ANNULARE OF THE HANDS AND FEET; TUBERCULIDS OF THE BODY. Presented by DR. T. J. RIORDAN.

A. L., a girl aged 6 years, was first observed to have an eruption in March, 1933. On the dorsal surface of the hands and feet were a number of discrete and confluent annular lesions varying in size from that of a pea to that of a dime, with infiltrated, slightly elevated borders. On the body there was a pinhead-sized, follicular, discrete papular eruption. The lesions were firm and had conical tops. A Mantoux test with 0.2 mg. of tuberculin was negative. A tuberculin test made at the Fifth Avenue Hospital was also negative. Roentgen examination revealed several areas of calcification at the roots of both lungs. There was no involvement of the parenchyma. Histologic examination of the hand revealed areas of tuberculous infiltration in the cutis and hypoderm. Histologic examination of the lesions on the body gave negative results.

The patient received six fractional doses of roentgen radiation at about ten day intervals between June 8 and September 11, which changed the clinical picture. There was marked improvement following treatment. There was a recurrence in the latter part of October.

DESTRUCTIVE OSTEITIS AND FACIAL PARALYSIS IN SECONDARY SYPHILIS. Presented by DR. DAVID BLOOM.

E. B., a colored girl aged 20, was admitted to the Bellevue Hospital on June 4, 1933, with a generalized and rather profuse eruption which did not itch and involved the face, the extremities and particularly the trunk. It consisted of groups of miliary and a few papules the size of a large millet seed. The eruption appeared ten days previous to the patient's entrance to the hospital.

On examination, a few pea-sized, whitish lesions on an erythematous base were found on one of the anterior pillars, but no lesions were present on the external genitalia. There was general adenopathy. The pupils were normal in size and

shape and reacted to light and in accommodation. The patellar reflexes were present. The temperature was slightly elevated and the patient felt weak.

The patient denied having felt a sore on the genitals, and the exact time of sexual intercourse could not be ascertained. A clinical diagnosis of miliary papular syphilid was made, which was confirmed by a strongly positive Wassermann reaction of the blood.

Following two injections of a bismuth compound and one of neoarsphenamine the patient complained of pain in the left acromioclavicular joint, over which there was seen an almond-sized, moderately firm swelling, erythematous, tender to pressure and painful on motion of the arm. She complained also of spontaneous pain in the left shoulder and arm, which was more pronounced at night. A roentgenogram revealed "destruction" of the acromial end of the clavicle. Under further antisyphilitic treatment, after four injections of neoarsphenamine and five of a bismuth compound a second roentgenogram was taken which showed distinct regeneration of the bone. On July 17, after having received five injections of neoarsphenamine and seven of a bismuth compound, the patient was discharged from the hospital and referred to the dermatologic clinic, where treatment and observation were continued. The patient soon discontinued attendance at the clinic but returned two months later, on September 19, with right facial paralysis. The right corner of the mouth drooped, and the mouth was pulled to the left; there was also lagophthalmos of the right eye. Following further antisyphilitic treatment the facial paralysis improved rapidly.

A roentgenogram of the acromioclavicular joint taken on September 26 showed "progressive regeneration of the acromial end of the clavicle," and the last roentgenogram, taken on October 19, was reported as showing an "arrested pathologic process."

NEW ENGLAND DERMATOLOGICAL SOCIETY

J. HARPER BLAISDELL, M.D., *Secretary*

Dec. 13, 1933

RUDOLPH JACOBY, M.D., *Presiding*

MULTIPLE BENIGN EPITHELIOMA OF THE SCALP (SO-CALLED TURBAN TUMOR, ENDOTHELIOMA CAPITIS, CYLINDROMA OF THE SCALP OR SPIEGLER'S TUMOR). Presented by DR. FRANCESCO RONCHESE, Providence, R. I.

This white woman, aged 72, born in Italy, has had an eruption for fifty years, the lesions having grown slowly and multiplied until they attained their present appearance. The patient's mother and a paternal aunt had a similar condition on the scalp. A daughter had a painful growth the size of a pea on the scalp.

There is an isolated tumor, embedded in the subcutis, in the occipital region. A bunch of tumors is present on the vertex. The growths vary in size from that of a pea to that of a walnut; they are packed together and form a lobulated mass about the size of a hen's egg. Pink-yellow discoloration is present. The tumors are firm. Some of them have been lacerated and have bled profusely when hairpins were stuck in. There has been no discomfort and no sign of rapid growth.

The Wassermann reaction of the blood was negative. Examination showed the urine to be normal. Roentgen examination of the skull revealed no pathologic changes. The blood chemistry showed 40 mg. of urea, 1.7 mg. of creatine and 160 mg. of sugar per hundred cubic centimeters.

Biopsy showed carcinoid of the scalp.

DISCUSSION

DR. FRANCIS P. MCCARTHY, Boston: These lesions, I understand, have been present in this location for about fifty years and have been subjected to considerable

trauma at times. From an examination of the section under the microscope, I believe them to be nevi or nevoid tumors, and the character of the growth suggests an origin in the sebaceous glands. Unfortunately the cells take the stain poorly, and it is difficult to arrive at a conclusion from the single section shown. I do not think that these are turban tumors of the cylindroma type.

DR. FRANCESCO RONCHESE, Providence, R. I.: Clinically this is a typical case of turban tumor or cylindroma of the scalp. The pathologic picture, however, is different from that in the cases described in the literature and quite puzzling. The majority of these growths have been described as ordinary basal cell epitheliomas. In this case there is a prevalence of prickle cells.

ACANTHOSIS NIGRICANS; TERTIARY SYPHILIS; SCIRRHOUS CARCINOMA OF THE STOMACH (INOPERABLE). Presented by DR. FRANCIS M. THURMON, Boston.

This white woman, aged 65, states that in September 1932, she first noticed a dark discoloration of the skin around the anus and the genitalia. Four months later (January 1933) extreme generalized pruritus developed, the itching being especially marked around the genitalia, gluteal folds and cubital fossae. Five weeks ago a diffuse swelling with redness and itching appeared over the arms and hands, which subsided but left the skin dry and scaling. During the past fifteen months there has been a gradual increase of dark pigmentation around the umbilicus. The patient has lost 15 pounds (6.8 Kg.) during the past five weeks, which she attributes to "indigestion," characterized by slight epigastric pain coming on approximately thirty minutes after the intake of food and lasting about half an hour. There have been no other gastro-intestinal symptoms except chronic constipation which has been present as long as she can remember. Five years ago she had an attack of "indigestion" similar to the present attack, and Dr. Flanders, of Roxbury, Mass., took a roentgenogram and told her that "the stomach did not empty as rapidly as it should."

The skin hangs loosely over the skeletal frame. It is dry, rough and scaling. Over the hands and arms it has a florid appearance and is definitely increased in thickness. There is increased pigmentation over the entire abdomen, and in the axillae and around the umbilicus there are areas approximately 5 cm. in diameter which are deeply pigmented, slightly raised and excoriated. Around the genitalia and anus there is an elevated area of firm black skin. A systolic cardiac murmur is present at the apex. The blood pressure was 110 systolic and 60 diastolic. Just to the left and slightly above the umbilicus a slightly tender, movable mass may be felt.

The urine was found to be normal. Gastric analysis revealed no free hydrochloric acid. The last aspiration was visibly bloody, and the benzidine test was positive. There had been no blood in previous aspirations. The blood count showed 71 per cent hemoglobin, 3,730,000 red cells, and 5,500 white cells, with 5 per cent eosinophils. The sedimentation rate of the blood was as follows: after twenty minutes, 7; after one hour, 32; after two hours, 65. The blood sugar was 110 mg. per hundred cubic centimeters, and the nonprotein nitrogen, 40 mg. The serum calcium was 8.33 mg. per hundred cubic centimeters. The icterus index was 6. The Hinton, Wassermann and Kahn tests were positive on three occasions. The basal metabolic rate was + 17.

Roentgen examination of the stomach revealed a scirrhous carcinoma 6 cm. in length starting just below the fundus and involving the stomach. The ascending aorta was bulging and showed a rubber-like pulsation. There was marked calcification of the aorta, the aortic notch and the descending aorta.

The patient has received a lotion locally to control the pruritus and bismuth, mercury and potassium iodide internally.

DISCUSSION

DR. E. LAWRENCE OLIVER, Boston: Such cases are rare. In adults they are usually associated with carcinoma in the stomach or elsewhere in the abdomen.

They are sometimes seen without an associated malignant process, especially in children. They are thought to be caused by pressure on the abdominal sympathetic nerves, though I do not know that that has been proved.

DR. FRANCIS M. THURMON, Boston: It is reported that about 80 per cent of such cases show a malignant growth in the abdomen. On the basis of the roentgen findings, I do not believe that there is any doubt that this patient's condition is inoperable scirrhous carcinoma of the stomach, and the involvement of the aorta probably is of syphilitic origin, with a superimposed sclerosing process. My idea is, since the growth is inoperable, to treat the patient for syphilis in the hope that the condition may be a gumma of the stomach. I have seen two cases of inoperable carcinoma of the esophagus proved histologically in patients with syphilis that responded to antisyphilitic therapy.

LEUKOPLAKIC VULVITIS; LICHEN PLANUS ATROPHICUS ON ABDOMEN AND CHEST (?); MYCOSIS FUNGOIDES (?). Presented by DR. HENRY BENJAMIN, Boston.

This white woman, aged 55, a layer of gold-leaf in a book bindery for twenty-five years, states that five years ago when the menopause occurred, pruritus vulvae developed. There was intense itching on the abdomen and breasts in February 1931, followed by a moist dermatitis one month later. The lesions then assumed their present appearance.

The skin of the perineum has an opaque, white appearance with superficial ulceration. On the breasts are four irregular, superficial, macular, pinkish-yellow lesions, slightly scaly and with some inflammatory reaction at the periphery. On the abdomen are irregular, thin, flat, red to violet lesions connected with thin white atrophic scar tissue, as well as fifteen round superficial ulcerations from 3 to 10 mm. wide. On the thighs are scattered groups of follicular excoriated lesions.

Biopsy on a specimen from the left breast on Dec. 2, 1933, showed irregular thickening of the stratum corneum and moderate downgrowth of the rete malpighii. There were moderate hyperkeratosis and infiltration of lymphocytes and a few eosinophils in the corium.

On Nov. 14, 1933, the Kahn test was negative. On November 9, a blood smear was found to be normal, and there were 4,100,000 red cells and 9,000 white cells per cubic millimeter.

The patient has received fifteen roentgen treatments of the vulva with slight relief. She has received no treatment over the abdomen and back.

DISCUSSION

DR. E. LAWRENCE OLIVER, Boston: The suggestion of scleroderma in the lesion under the fold of the abdomen and where it hangs over is extremely interesting. The lesion certainly felt much like scleroderma. It seems to be deep-seated, more than one would expect in atrophic lichen planus. The lesions on the breast do not look anything like scleroderma to me. They are sharply defined, slightly raised and erythematous. I am puzzled by the condition. It does not seem to me that the diagnosis of lichen planus atrophicus covers these manifestations. I wonder if some endocrine change is not going on.

DR. VINCENT RYAN, Providence, R. I.: This patient presents three distinct dermatologic conditions. I cannot diagnose the lesions on the breast. The history is that they are recurrent and disappear without treatment. I think that the lesions on the abdomen are the result of trauma. They look like scar tissue. The patient gives a history of ulcers forming in the scar tissue. Constant scratching over a long period can cause such a change in the tissues.

DR. E. MYLES STANDISH, Hartford, Conn.: I have no opinion to offer, but I should like to mention that the lesions seem to be absolutely symmetrical. Whether that indicates an endocrine disorder I do not know.

DR. FRANCIS P. MCCARTHY, Boston: I was one of the group that agreed to the diagnosis of lichen planus atrophicus. One diagnosis came into my mind, however, which was not mentioned, namely, lupus erythematosus.

DR. FREDERICK S. BURNS, Boston: I have no definite diagnosis to propose for the lesions on the breast. They interest me very much morphologically. They seem to be definitely polycyclic, with a tendency everywhere to assume atrophic involution. The condition suggests lichen planus atrophicus. I find it difficult to reconcile the lesions with lupus erythematosus, in spite of the atrophic features.

DR. HENRY BENJAMIN, Boston: Several things came into my mind in presenting this case. The features that justify the diagnosis of lichen planus are the flat irregular, angulated lesions on the abdomen and the intense itching.

Mycosis fungoides was mentioned as a possibility because of the history of intense itching and because the morphologic characteristics are somewhat consistent with that diagnosis. The lesions on the abdomen suggest a precancerous condition.

In view of the contact with gold for twenty-five years, one might bring up the question of gold dermatitis. However, I do not think the influence of gold plays an important part. Gold intoxication resembles other metallic intoxications in the damage produced in the liver and kidneys and also the metallic line on the gums and the stomatitis that occur. None of these symptoms are present in this case. Cutaneous lesions caused by gold have a tendency to become pigmented. Moreover, gold tends to produce dermatitis on unpigmented areas, which is not the case here.

There may be two separate conditions present on the chest and abdomen. The lesions on the abdomen may be a dermatitis due to circulatory stasis. They are located on the most dependent part of the pendulous abdominal wall and may be caused by chronic passive hyperemia. The scarring and infiltration are consistent with that conception. I cannot offer any diagnosis for the lesions on the breasts.

DR. JOHN G. DOWNING, Boston: In discussing this woman's history, it has not been brought out that she worked for years about 6 feet (2 meters) from intense heat. The parts most affected are the prominent dependent areas, the lower parts of the breasts and abdomen. She is very fat, and the parts affected are in the regions where there is the most moisture and perspiration. I think that the eruption started as erythema due to heat, exaggerated by obesity and excessive perspiration. Another element that should be considered is that the patient received a series of roentgen treatments over the vulva, the most prominent area exposed to radiation, which may have resulted in atrophy of the skin of the abdomen.

DR. WILLIAM J. MACDONALD, Boston: I suggest that Dr. Benjamin make a biopsy. If the condition is lichen planus, a biopsy will show the typical changes. If it is an early mycotic condition, that will undoubtedly be revealed. I do not know what the lesion on the lower part of the abdomen is, but with Dr. Downing I believe that exposure to roentgen rays may have caused it. It is possibly a malignant process, and I suggest that Dr. Benjamin report the microscopic observations.

NOTE.—The observations at biopsy were not consistent with lichen planus.

LICHEN PLANUS AND SYPHILIS. Presented by DR. WALTER T. GARFIELD, Boston.

This colored boy, aged 7 years, on June 12, 1933, came to the ophthalmologic department totally blind. A diagnosis of traumatic keratitis with marked haziness of the cornea was made. The Kahn test was positive. The patient was referred to the dermatologic department, where he received four injections of neoarsphenamine. He was discharged to the outpatient department on August 15. A blood test was positive, and he was given fifteen more injections of neoarsphenamine. The last treatment was given on December 5. His father states that lesions

on the hands, wrists, ankles and feet developed about a week ago. There has been some itching.

There are now purplish, shiny, flat-topped, straight-sided, square-cornered lesions on the wrists, the backs of the hands, the ankles and the dorsa of the feet.

The ocular condition has cleared up under antisyphilitic treatment.

DISCUSSION

DR. WALTER T. GARFIELD, Boston: This case is interesting because the lesions developed while the patient was being treated with arsphenamine, and arsenic is supposed to be useful in the treatment of lichen planus. Another interesting point is that when he first came to the clinic, he was referred from the ophthalmologic department with a diagnosis of "interstitial keratitis and a positive Wassermann reaction." Both of the parents have had repeated Wassermann and Kahn tests, all of which were negative. Three other children have also given negative reactions. At about the age of 2 years, owing to family conditions, the child was sent to the father's sister-in-law. It was later found, according to the father's statement, that both the sister-in-law and her husband had active syphilis at that time. The question came up whether the patient may have acquired syphilis with interstitial keratitis.

DR. RUDOLPH JACOBY, Boston: It is interesting to consider whether a boy aged 7 years can have acquired syphilis with interstitial keratitis the only symptom.

DR. E. MYLES STANDISH, Hartford, Conn.: One cannot overlook the fact that the simplest explanation of the pigmentation is that it is due to treatment with neoarsphenamine.

DR. FRANCIS M. THURMON, Boston: I have seen several cases of acute interstitial keratitis in patients with acquired syphilis.

DR. AUSTIN W. CHEEVER, Boston: I believe the patient has congenital syphilis. I have never seen an unequivocal case of acquired syphilis with interstitial keratitis. However, acquired syphilis at this age is not unusual, as a result of fondling or kissing by the relatives, and it can exist without showing any signs.

DR. WILLIAM P. BOARDMAN, Boston: Derby reported a very large series (500) of cases of interstitial keratitis in which he found only two which he thought were due to acquired syphilis. In this child the shape of the bones of the head and the frontal and parietal bosses suggest congenital syphilis. I am inclined to say that if the child has acquired syphilis, he has had some other form of keratitis. I have never seen any such angular, bluish, flat, papular lesions as the result of arsenic. The distribution is entirely consistent with lichen planus.

DR. J. L. GRUND, Boston: The occurrence of a lichenoid or lichen planus-like eruption following arsphenamine therapy is extremely interesting. At present, the most that can be said of this patient's lesions is that they are lichenoid. Buschke and Freymann first described in 1921 a lichen planus-like eruption which developed following arsphenamine treatment. In 1922, McCafferty described a similar case. Buschke and Freymann were of the opinion that the appearance of the eruption was not coincidental but directly attributable to the arsenical. They found that the eruption either remained refractory or became worse with persistence of the treatment. Alswhede later offered the opinion that such eruptions do not represent a specific dermatosis but are a form of cutaneous reaction developing on a constitutional basis. In connection with the foregoing consideration it is of added interest to point out that a lichenoid or a lichen spinulosus-like eruption may occur not only after arsphenamine treatment (Stauffer) but following infection. Jadassohn first linked its development with tineal infection of the scalp. Becker described a case in which it became manifest following the local administration of diphtheria toxin in the carrying out of a Schick test. It has even been reported following the ingestion of phenolphthalein (Mitchell). Its presence usually denotes the development of a constitutional reaction which is directly due to the introduction of a toxin or a chemical which acts in an irritating or sensitizing capacity.

PURPURA ANNULARIS TELANGIECTODES (MAJOCCHI). Presented by DR. M. MAURICE TOLMAN, Chelsea, Mass.

This white woman, aged 56, first noticed a lesion on her right thigh about ten weeks ago. It appeared as a group of spots which grew by peripheral extension from the size of a five cent piece to the present size. About two weeks later other spots began to appear. The latest spots, those on the forearm, appeared two weeks ago. The eruption has not caused any symptoms. The patient has had no local or other treatment. She believes that the original lesion is fading. The general history is unimportant.

On the inner aspect of the right thigh is a circular lesion about 2 inches (5 cm.) in diameter. The center is rather clear and slightly pigmented, and the margin shows brownish, punctate spots. Just away from this lesion are several areas similar in color but more irregular in outline and resembling cayenne pepper spots. There are several smaller lesions on the back of the same leg and on the other leg. There are also two similar lesions on the flexor aspect of the left wrist.

The blood count showed 4,400,000 red corpuscles, 7,800 white corpuscles and 80 per cent hemoglobin. The blood smear was not remarkable. The urine was normal. Serologic tests have been made, but the results have not been reported. A biopsy has not been made.

DISCUSSION

DR. FRANCESCO RONCHESE, Providence, R. I.: The condition is of too short duration to be purpura annularis, telangiectodes, and it shows no evidence of annular formations. It may be an early case of poikiloderma atrophicans vasculare.

DR. E. MYLES STANDISH, Hartford, Conn.: As I recall the case originally reported by Dr. MacKee, purpura annularis telangiectodes begins as cayenne pepper spots which soon form a lesion clearing centrally. The lesion may be scaly or superficially atrophied. I recall a number of lesions larger than a pea, but I have never seen such a large one as this man has, and I do not believe lesions of this size occur. The only thing that fits in with this condition is that the patient has cayenne pepper spots and telangiectasia; however, these can occur in other diseases. I do not think that this is a case of Majocchi's disease.

LUPUS VULGARIS (?). Presented by DR. FRANCIS P. MCCARTHY, Boston.

This white girl, aged 15, gives a history of intertriginous lesions of the commissures of the lips which have been present on the right side for a year and on the left for five months, with gradual development of an ulcerated, painless lesion extending to the upper lip.

There is now a raised, crusted, indurated, ulcerated lesion the size of a dime. The surface bleeds readily. There is no enlargement of the cervical glands. There is an intertriginous fissure in the right labial commissure.

A report has not been received on the Wassermann test and the biopsy. Cultures have been made but have not been reported on.

The patient has received no treatment.

DISCUSSION

DR. WILLIAM B. COHEN, Providence, R. I.: I could not see any apple jelly-like nodules that would lead me to make a diagnosis of lupus vulgaris.

DR. RUDOLPH JACOBY, Boston: A biopsy specimen was taken but has not been reported on. I presume that most of the members feel that the diagnosis hinges chiefly on the microscopic observations.

DR. AUSTIN W. CHEEVER, Boston: I am not ready to make a definite diagnosis, but I see no objection to lupus vulgaris. One should not fail to notice that the child almost certainly has congenital syphilis. Both upper central incisors and the left lateral and right central lower incisors are involved, and there is marked anterior bowing of the shins.

DR. FRANCIS P. MCCARTHY, Boston: I hoped to have a biopsy report today, but it is not quite finished. I should like to receive suggestions as to methods of treatment to be used in the event that the condition proves to be a tuberculoma or lupus vulgaris.

DR. WILLIAM J. MACDONALD, Boston: I should remove the lesion with the coagulating current.

DR. FRANCIS P. MCCARTHY, Boston: The question of cosmetic results is important.

DR. JOHN G. DOWNING, Boston: I have obtained good results in treating two patients by boring into the lesions with a wooden applicator which had been dipped in mercuric nitrate. A patient with a lesion on the face was relieved by this method; however, the lesion recurred, as in all tuberculous cases.

DR. WILLIAM J. MACDONALD, Boston: I do not think that the cosmetic result should be considered. The correct procedure is drastic removal.

DR. J. HARPER BLAISDELL, Boston: I have seen nothing superior to the old-fashioned but effective curetting of such lesions. This method was used by Dr. Burns and me a great many years ago. One can curet the lesion down to a perfectly firm, hard base, paint the surface with iodine and follow this with roentgen irradiation if one wishes to do so. The cosmetic result is excellent.

DR. E. LAWRENCE OLIVER, Boston: The Hermannsdorfer-Sauerbruch diet is worth trying.

DR. RUDOLPH JACOBY, Boston: Has any one had any particular success with any treatment?

DR. CARL D. SAWYER, Providence, R. I.: Has any one had experience with the use of potassium permanganate in treating lupus vulgaris on the face? About six years ago an article appeared in which potassium permanganate was advocated. It is employed by curetting off the crusts and applying to these areas powdered potassium permanganate, which is left on over night. I tried this method in one of my cases and obtained a good result. This patient has a small area of involvement, and it could be tried.

DR. FRANCIS P. MCCARTHY, Boston: The biopsy report has just been handed to me. It shows the lesion to be a tuberculoma.

SCLERODERMA. Presented by DR. RUDOLPH JACOBY, Boston.

M. B., a colored woman aged 33, states that four years ago swelling of the fingers and hands occurred. The skin of the fingers became darker, and the fingers were hard to move. She noticed loss of pigment on the arms. Two years ago she noticed that the tissue of the arms was hard. Two or three months ago the upper part of the chest became similarly affected. She was treated for rheumatism for years. She was told that she had arsenic poisoning, for which she received intravenous therapy. Her face also is becoming affected.

The fingers of both hands are cold, and the tissues are hard, causing restriction of motion. The skin of the fingers is atrophied. There are mottled areas of depigmentation on the upper and lower parts of the right arm and similar areas on the upper part of the left arm. The areas mentioned show marked hardening of the tissues. There is depigmentation of the right side of the upper part of the chest, as well as marked hardening of the tissues of the entire upper part of the chest. There is beginning depigmentation on the upper part of the forehead near the hair line. There is a trophic disturbance as a result of a scar on the right index finger.

The Wassermann and Kahn tests of the blood were negative. A tuberculin test (Mantoux) was positive. The blood count showed 80 per cent hemoglobin, 4,130,000 red cells, 6,850 white cells, 51 per cent polymorphonuclears, 39 per cent lymphocytes, and 3 per cent eosinophils.

The patient has received six massage treatments in the physical therapy department.

Following the tuberculin test she had severe iritis in both eyes.

She is presented for suggestions as to treatment.

DISCUSSION

DR. RUDOLPH JACOBY, Boston: The tuberculin test (Mantoux) was positive with both bovine and human strains. Immediately after this, severe iritis and photophobia developed. The question arose whether this was a factor in the etiology of scleroderma. I should like suggestions as to treatment. Dr. Oliver suggested massage for a patient observed recently. I sent this patient to the physical therapy department, where she had six systematic massage treatments, without relief. She has atrophic changes of the fingers suggesting Raynaud's disease. My interpretation is that those lesions are merely an atrophic disturbance resulting from the scarring. I am considering giving the patient a preparation of pancreatic substance, and I wonder if any one has had experience with this medication.

DR. WILLIAM P. BOARDMAN, Boston: The fact that the patient has tuberculosis has a direct bearing on the case. In going over the literature I found that almost every infectious disease has been followed by scleroderma and also that many toxic noninfectious conditions have been followed by scleroderma. This patient evidently has tuberculosis, and that may be the underlying factor. For that reason I suggest active treatment of the tuberculosis in the usual way. I suggest treatment in a sanatorium to see if it will help the scleroderma as well as the tuberculosis.

DR. E. MYLES STANDISH, Hartford, Conn.: I saw this patient last July. As I remember the history, she had early symptoms and signs of involvement of the hands that made me think the condition began with Raynaud's syndrome. She lived in the country and had been drinking well water. The question of the intake of lead and arsenic came up. I referred her to her physician and advised that the urine be checked for elimination of arsenic. I advise that before treatment this test and also a basal metabolism test be made and that Dr. Smithwick's advice be asked as to whether or not it is too late to perform sympathectomy for the relief of the condition of the hands. I had a patient who went to the Mayo Clinic for this treatment without result; I have given her a preparation of pancreatic substance, and the scleroderma has gradually progressed.

DR. RUDOLPH JACOBY, Boston: The patient has not been given a complete physical or roentgen examination because she has been so ill with the iritis. What can be done for such patients when constriction of the fingers develops?

DR. E. MYLES STANDISH, Hartford, Conn.: Dr. Addison's sympathectomy is supposed to prevent such contraction in early cases of Raynaud's syndrome.

PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA (HABERMAN)? Presented by DR. BERNARD APPEL, Boston.

This white man, aged 65, a grocer, states that ten weeks ago a nonpainful, nonitchy "cigar burn" lesion developed on the lower lip, which lasted about two weeks and then healed completely without a scar. Gradually a similar eruption appeared all over the body in series of successive lesions, some grouped and some discrete. They were nonitchy and started as blisters, which lasted a few days and then dried into bloody crusts. In a few days the crusts fell off, leaving smooth pink scars. The older scars are surrounded by brown stains. Two weeks ago the patient had a sore throat and sore gums for two days. There has been no feeling of general illness and no fever. Since the age of 14, he has had constant pruritus, especially on the buttocks and scapulae, and there have been crusts on the scalp. The lesions have developed only after scratching.

There is now a nonitchy, nontender generalized eruption, which is more profuse over the extremities. The lesions vary from a few millimeters (early) to 1 cm. (late) in diameter. Some are small, yellowish papules; others are of abraded vesicles, leaving a bloody, crusted adherent scale the removal of which leaves a small punched-out, crater-like shallow ulcer. Some of the larger lesions are rupial. Some, especially on the palms and soles, are keratotic. An occasional pustule may be seen. The whole picture resembles moderately severe and active secondary syphilis. There is some cervical adenitis, which is nontender.

The Wassermann reaction of the blood on Nov. 23, 1933, and on Dec. 1, 1933, was negative. The urine was normal. A blood count showed normal values for red and white cells. A smear was normal.

The patient has been given various ointments and lotions by his family physician with no apparent effect. Fowler's solution has been administered in a dose of 4 minims (0.24 cc.) three times a day, and he has also received tablets of mercurous iodide (¼ grain [0.015 Gm.]) three times a day, with no apparent effect.

DISCUSSION

Dr. William J. MacDonald, Boston: I make a tentative diagnosis of erythema multiforme bullosum et vesiculosum.

Dr. Austin W. Cheever, Boston: I tried to trip the patient into admitting taking some kind of drug. I could not do it. The eruption looks like an iodide rash.

Dr. John G. Downing, Boston: The picture does not agree with that in the cases of pityriasis lichenoides et varioliformis that I have seen. First, the distribution is not typical. There are a considerable number of lesions on the back and the palms. Second, the size of the lesions does not correspond with that in the cases that I have seen. Third, the various stages are not present. The only eruption consists of large, crusting, hemorrhagic lesions surrounded by a faint zone of erythema. These lesions do not show the characteristic scarring that generally follows pityriasis lichenoides et varioliformis. The lesions in that disease are more of the varicella type. The lesions on the hands in this case are more of the type seen in septic conditions.

Dr. J. Harper Blaisdell, Boston: The primary lesion in this case is a pustule, which becomes necrotic and heavily crusted. In the absence of proof to the contrary, I think the eruption is best explained by iodism.

Dr. E. Lawrence Oliver, Boston: Can the urine not be tested for iodides?

Dr. Francis P. Thurmon, Boston: Although there is little doubt in my mind as to the correctness of the diagnosis, I have seen two cases of malignant secondary syphilis with similar sharply circumscribed lesions. I believe that syphilis has been ruled out on the basis of repeated Wassermann tests. I do not think syphilis should be ruled out on the basis of a repeatedly negative Wassermann reaction alone.

Dr. J. Harper Blaisdell, Boston: It is my impression that the rupial syphilitic lesion is convex like an oyster shell. These crusts are concave with a depression in the middle. Is that impression correct?

Dr. Austin W. Cheever, Boston: The condition does not impress me as secondary syphilis. I should not rule this diagnosis out on the basis of the negative serologic reactions, nor should I consider syphilis seriously even if the Wassermann reaction were positive. The primary lesion is a pustule arising from a somewhat erythematous base. There are several pustules on the upper parts of

the arms and the palms. The crusting is not rupial, not heaped-up. A rupial lesion starts as a small crust, and another forms under it, raising it up like an oyster shell. I rule this diagnosis out because of the clinical appearance. It is possible to have rupial syphilis with a negative Wassermann reaction.

DR. J. HARPER BLAISDELL, Boston: What about a pustular syphilid?

DR. AUSTIN W. CHEEVER, Boston: I have never seen a vesicular syphilid in an adult or a pustular syphilid on the palms. I have seen pustules that were probably syphilitic on the back.

DR. E. LAWRENCE OLIVER, Boston: It seems to me that the primary lesion is a vesicle, not the pustule that would be present in secondary syphilis. The condition looks like a superficial vesicular eruption with secondary infection. If the patient had secondary syphilis, he would not be as well as he is. I think that iodide could produce such a picture. I did not inquire into his habits with regard to the use of alcohol.

DR. FRANCIS P. MCCARTHY, Boston: I investigated the history as to use of alcohol. At the age of fourteen the patient "took the pledge," and he has not touched alcoholic drinks since. He has never taken any medicine. He has no bad habits of any kind, according to his history.

DR. WILLIAM P. BOARDMAN, Boston: I do not think that iodide eruptions present such symmetry as this, with involvement of both palms and both soles. The distribution is more marked on the flexor surfaces of the extremities than on the extensor surfaces, and here again there is a symmetry which I do not think would be observed in an iodide eruption. I have never seen a case of pityriasis lichenoides et varioliformis, but the distribution of the lesions coincides exactly with the sites described as usual in the articles published in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY in 1930, namely, the body and the extremities with slight accentuation on the flexor surfaces.

DR. BERNARD APPEL, Boston: I have never seen a definitely proved case of pityriasis lichenoides et varioliformis. As nearly as I can remember, this is the first time that I have definitely made a diagnosis of secondary syphilis to the patient before laboratory confirmation. Much to my chagrin, the report on the Wassermann test was negative, and the results of repeated examination were also negative. The patient was kind enough and intelligent enough to forgive my first diagnosis and has been cooperative in my attempt to determine the cause. I thought of the diagnosis of pityriasis because I remember reading the reports of the cases that were strikingly described by Senear and Oliver in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**23**:12 [Jan.] 1931) after having been shown at the Annual Session of the American Medical Association in 1930. I feel for several reasons that this patient probably does not have syphilis. In the first place, though the Wassermann test is not as sensitive in some cases as in others, when syphilis produces such a violent picture as that present in this case there should be enough reagins in the blood to give a positive reaction. Second, if he had syphilis severe enough to produce such a violent eruption, he would certainly have some other symptoms. As to the size of the lesions, I have before me two articles, one by Wise and the other by Senear and Oliver, in both of which it is stated that the size of the lesions may vary from that of a pinpoint to that of a French pea, which I think, on the basis of my garden experience, is about the size of an American pea. The primary lesions in this case are vesicles, which soon become pustular. The patient shows a few clear vesicles on his chest today. One other interesting feature not mentioned in this discussion is the chronic itching which the patient has had since the age of 14. This itching does not occur until he has scratched a lesion vigorously. The itching areas are principally over the buttocks and the scapular regions. The skin is so sensitive that if he carries a bunch of keys in his pocket he has to scratch that side of his thigh at night. It

seems to me more than a coincidence that there is no relation between this chronic itching and pityriasis lichenoides et varioliformis.

DR. JOHN G. DOWNING, Boston: The diagnosis that I made originally was scabies with secondary sepsis.

SPOROTRICHOSIS. Presented by DR. JOHN G. DOWNING, Boston.

This white boy, aged 14, was admitted to the dermatologic clinic on Nov. 4, 1933, with chief complaints of a swollen right index finger and swollen lumps on the right arm of two months' duration. Four months ago he injured his right index finger on a nail. He attempted to clean the abrasion with a penpoint and then bandaged it for two weeks. At that time, swelling and redness appeared at the metacarpophalangeal joint. Since that time the lesions have been growing slightly larger, have more or less coalesced and from time to time have discharged a creamy pus. A moderate amount of pain has been associated with the lesions. About two months ago a hard, tender swelling appeared just below the right elbow on the medial anterior aspect of the forearm. Following this, other lumps appeared on the medial aspect of the upper part of the arm. These were all similar, being red, tender and rather hard and varying from 1 to 3 cm. in diameter. Vomiting has occurred four or five times, and there have been some headache and a slight dry cough. The patient has lost about 14 pounds (6.5 Kg.) during the past six months. His history reveals that he had a tonsillectomy five years ago. There are no other significant features. There have been no symptoms of pulmonary disease except the slight cough mentioned. The patient was born in Boston and has always lived there.

The boy appears healthy. His face shows many comedones, papules and pustules (typical acne vulgaris). There are a few verrucae on the fingers and a herpetic lesion on the upper lip. The chief point of interest is the involvement of the right arm. On the index finger is an indolent, infiltrated, somewhat verrucous lesion 2 cm. square over the proximal phalangeal joint. It excretes a serous, purulent discharge. At the base of the finger there is a group of nodular lesions which discharge a thin, watery fluid. On the radial aspect of the right forearm is a slightly tender, somewhat tense nodule the size of a grape. Just above the antecubital space on the medial aspect of the upper part of the arm there are scattered four similar nodules. These are dusky pink and only slightly tender.

The blood count showed 19,600 white blood cells and 90 per cent hemoglobin (Tallqvist). The urine was normal. The Kahn test was negative. Cultures were made in the hospital but showed no growth. Cultures made in the outpatient department on Nov. 7, 1933, showed a mature colony of the fungus isolated from the pus with a central knob and a surrounding area of hyphae close to the agar, radially furrowed and gray-brown at least in parts. A hanging drop culture showed branching, septate hyphae and egg-shaped conidia, apiculate at one end, attached singly along the sides of the hyphae or in clusters at the ends of short conidiophores. The fungus was a sporotrichum, probably the strain described as Sporotrichum Beurmanni.

Biopsy was decided against as it was feared that surgical intervention might further the spread of infection.

About one week after admission to the hospital, the lesion on the right forearm opened and seemed about to break down. In general, the lesions remained about the same under palliative treatment with boric acid ointment. Application of 1 per cent iodine every six hours was started on Nov. 14, 1933, and the administration of a saturated solution of potassium iodide was begun on November 16, the doses being increased so that at the time of discharge the patient was receiving 28 drops three times a day without untoward reaction. During the last week in the hospital, he had a mild respiratory infection which rapidly cleared when he was kept in bed.

NEW YORK DERMATOLOGICAL SOCIETY

R. H. RULISON, M.D., *Secretary*

Regular Meeting, Dec. 19, 1933

EDWARD R. MALONEY, M.D., *President*

SPIEGLER-FENDT'S SARCOID. Presented by DR. GEORGE M. MACKEE.

This housewife, aged 58, when first observed on Nov. 24, 1933, complained of a steadily enlarging mass on her right breast which had been present for three months. There have been no subjective symptoms.

Situated 2.5 cm. below and mesially to the right nipple is a bright red, oval, elevated mass 3 by 2 cm., with the long axis lateral. The surface is smooth and irregular, and near the inner border are several papules the size of a millet seed, more or less translucent and shiny. On palpation the tumor, while firm, does not have a cartilaginous or even a fibrous consistency. The sensation is rather that of feeling soft rubber.

Beyond the distal border of the mass is a group of palpable, slightly reddened papules the size of a pinhead the color of which is obliterated on diascopic pressure, leaving whitish-yellow stains, possibly resembling the color of boiled sago, although a more definitely yellow tint is also present. A group of similar discrete pinhead-sized lesions occupying an area 2 cm. in diameter is present on the wall of the chest 3 cm. mesial to the inner border of the large mass. The discrete papules have rounded tops and are without umbilication. When viewed in a reflected light the lesions are distinctly shiny.

Examination of sections from a biopsy specimen revealed a distinct circular, cellular mass extending from the midcutis to the epidermis. In the remaining tissue in the upper cutis and the subepidermic region there was considerable cellular infiltration, and the connective tissue framework was broken up. The rete pegs and papillary bodies were almost entirely lost. The mass was composed of wandering connective tissue cells and small round cells. A moderate number of small blood vessels were also present. The cellular infiltration of the remaining tissue was also composed of wandering connective tissue cells and small round cells. The connective tissue exhibited granular degeneration.

Treatment has consisted of the administration of Fowler's solution in increasing doses and roentgen irradiation (360 roentgens unfiltered on December 15).

DISCUSSION

DR. J. FRANK FRASER: Under the microscope the picture is not the usual one of sarcoid but that of lymphoblastoma or of reticular cell lymphosarcoma.

DR. GEORGE M. MACKEE: Years ago, when the histologic characteristics of tumors were under controversy, there was considerable difference of opinion as to whether a growth such as this one was sarcoma. Finally, as I understand it, Spiegler and Fendt used the word "sarcoid" to separate the condition from sarcoma because some investigators did not think that it was a true neoplasm or sarcoma. One still has to contend with the term sarcoid. Of course, the growth is nothing like the Boeck and the Darier-Roussy sarcoid, which belong in the tuberculosis group.

In studying the slides I did not get the impression that the mass was a true sarcoma or lymphosarcoma or even a true neoplasm. It appeared to be identical with or at least similar to the Spiegler-Fendt sarcoid. The results of roentgen treatment may prove enlightening. It is my impression that Spiegler-Fendt sarcoid does not yield readily to roentgen irradiation. Perhaps that is not a fair statement to make, because very few patients with that condition have been treated with the roentgen rays. On the other hand, lymphosarcoma is, I believe, much more

amenable to such treatment. Therefore, if this eruption clears up rather readily under roentgen treatment, I shall be inclined to make a diagnosis of sarcoma rather than of the Spiegler-Fendt sarcoid.

MELANOMA: RESULT OF TREATMENT AT THE END OF FOUR YEARS. Presented by DR. HOWARD FOX.

T. de R., a woman aged *26*, was presented before the society on Nov. *27*, 1929, at which time she showed a pinhead-sized, bluish, smooth spot on the tip of the nose. This was excised, and the tissue was examined microscopically. The histologic report by Dr. Highman was that the lesion was a melanosarcoma. There has been no recurrence in the past four years, and the cosmetic result of the operation, performed by Dr. Jay D. Whitham, was excellent.

DISCUSSION

DR. WALTER J. HIGHMAN: Unquestionably, from the histologic appearance four years ago, the lesion was a melanotic spindle cell sarcoma, or rather a young spindle cell sarcoma, probably fibroblastic. It was evidently not highly malignant. I am beginning to wonder whether all melanomas are as frightful as one has been led to think. Here is evidence to the contrary. I recently saw in consultation a boy of 8 years who has a growth on the forehead which obviously started from a nevus and which has grown rapidly in the past six months. There is considerable controversy as to the malignancy of the growth, and one or two good general pathologists doubt that it is a melanoma. To me it looks like a melanoma. I wonder what the proper criteria of malignancy are, histologically and clinically, and if the prognosis is always as serious as one has been led to believe.

DR. J. FRANK FRASER: I agree with the remarks of Dr. Highman. The diagnosis of melanoma which he made four years ago was correct. I recall a case which came under observation several years ago in which the histopathologic diagnosis was malignant melanoma. The patient was still in good health at the end of five years. One must conclude that such tumors are not always as malignant as they are supposed to be.

DR. C. M. WILLIAMS: One sees a great many cases of melanotic tumors of the blue-black type which remain unaltered for a great many years and which are clearly not malignant at that stage. It is also true that some of these growths are malignant, spread rapidly and are fatal. I intended to ask the pathologists whether they can tell which growths will be malignant and which will not, but they have already answered that they cannot tell.

DR. E. F. TRAUB: Some of the confusion, no doubt, has arisen because the clinical differentiation between the blue nevus and the so-called slate-black mole is not well recognized. The slate-black mole is looked on usually as a definite precursor of a malignant growth (some authorities assume its malignancy from the start). It develops into a melanocarcinoma or a nevocarcinoma. The blue nevus, on the other hand, is probably encountered as frequently as the slate-black mole but rarely becomes malignant. When degeneration does take place, the resultant lesion is a melanosarcoma.

DR. WALTER J. HIGHMAN: Histologically there is only one criterion of value in determining the malignancy of a tumor. If there is a good deal of associated inflammation and the tumor cells seem to be infiltrating into the neighboring lymphatics, these findings may indicate malignancy.

DR. J. FRANK FRASER: The main feature of a malignant melanoma is lymphatic infiltration. Another point is the degree of hyperchromatism in the nuclei and the number of mitotic figures. When one sees malignant cells invading the lymph channels, that is evidence of metastasis.

DR. HOWARD FOX: There can be no doubt that it is difficult to prophesy the outcome in cases of melanoma. Some growths are rapidly fatal, while others

remain unchanged for long periods. I thought it of interest to show this patient who has apparently been cured in comparison with the patient presented last month who had a melanoma of the nose on which a cutaneous horn had developed.

INFECTION WITH THE DUCREY BACILLUS WITH ECZEMATOUS ERUPTION. Presented by DR. FRED WISE.

This man, aged 39, married, was first examined on Nov. 4, 1933, at which time his eruption was of seven weeks' duration. The family and personal histories were unimportant except that he had asthma.

The eruption began about the middle of September, 1933, as a weeping and itching spot behind the corona of the penis. It soon spread to involve the entire glans penis and the anterior portion of the shaft; at the same time, a separate patch of weeping dermatitis appeared on the anterior surface of the scrotum. This was sharply defined and elevated.

Examination revealed, in addition to the eczematous changes, several pinhead-sized ulcers below the urethral meatus. Smears from these ulcers revealed the presence of the Ducrey bacillus. The Wassermann, Kahn and Kline precipitation tests were negative; a patch test with Dmelcos vaccine was strongly positive, but an intradermal test was negative. Local therapy of many kinds, including several roentgen treatments, failed to influence the eruption on the genitals. On November 11, a 3 per cent iodoform ointment was applied, resulting in improvement of the genital lesions; however, shortly afterward, an eczematous eruption appeared on the eyelids and extremities, possibly caused by absorption of the iodoform. On November 27, a small node appeared in the right inguinal region.

DISCUSSION

DR. C. M. WILLIAMS: The fact that the Ducrey bacillus was found in this case is not necessarily diagnostic. I think that this organism is found sometimes as a saprophyte. I noted in the last reading that I did on such cases that the authorities have abandoned the belief in the specificity of the Ducrey bacillus in these cases. The ulceration of true chancroid I should expect to be much deeper. In this case the ulceration is superficial. Moreover, there is a great deal of production of new tissue, which is against the rule for chancroid. The nodules are eroded, perhaps, but certainly not ulcerated. The condition reminds me very much of that of a man whom I saw at the Skin and Cancer Hospital about five years ago, in whose case a half-dozen diagnoses were made before death, when his condition was recognized to be pemphigus. I cannot make a positive diagnosis in this case.

DR. HOWARD FOX: With the exception of the ulceration, the lesions are precisely like those in a case that I presented at the last meeting, in which there was a diffuse, shiny infiltration of the glans, prepuce and penis in a patient with ringworm of the feet. No one was able to suggest a diagnosis of the penile lesion. There was no improvement in my case after a considerable amount of roentgen therapy, but the patient eventually improved after the use of chrysarobin ointment.

DR. WALTER HIGHMAN: I have observed cases such as this one. The Ducrey bacillus appears to be an anaerobe. When the Ducrey bacillus is present and the lesion is hard to get under control, I suggest that one use hydrogen dioxide or potassium permanganate and have the lesion exposed to the air as much as possible.

SARCOID. Presented by DR. FRANK C. COMBES.

This woman, aged 50, presents an eruption confined to the neck and shoulders and the extensor surfaces of the forearms. It is of eighteen months' duration and has gradually assumed its present extent. Similar lesions previously existed on the face and the backs of the hands but disappeared spontaneously, leaving only a suggestion of atrophy.

She presents a well defined erythematopapular eruption about the neck, extending for about 10 cm. onto the chest and back. Activity is present only at the borders, where there are many closely packed, flattened, erythematous and colorless papules, some of which are depressed in the center. They vary in size to about 0.5 cm. in diameter and are superficial. The entire lesion is free from crust or scale, and there are no patulous follicles. Where the process has resolved it has left a thin, atrophic, white scar. There is no clinical evidence of caseation necrosis. There are similar patches on the extensor surfaces of both forearms, about 5 by 10 cm. in diameter.

Roentgen examination of the lungs showed arrested tuberculosis. The Wassermann reaction of the blood was negative.

The histologic interpretation of sections from the back and the right forearm was that the condition was sarcoid.

DISCUSSION

DR. FRED WISE: My first impression was that the eruption is lupus erythematosus. However, I shall have to accept the diagnosis of sarcoid if the histologic observations support it.

DR. WALTER J. HIGHMAN: I think that the condition is sarcoid, lichenoid in appearance.

DR. GEORGE M. MACKEE: I think that clinically the condition is sarcoid. The fundamental lesion is a papule or a very small nodule. These lesions are numerous and rather lichenoid and coalesce in places, forming plaques. That is not the picture of lupus erythematosus. Histologically I think that lupus erythematosus can be ruled out definitely and that the picture corresponds fairly well with what is understood as sarcoid. Therefore, I should call it a lichenoid sarcoid.

DR. HOWARD FOX: I agree with Dr. MacKee in his diagnosis of lichenoid sarcoid, one of the recognized types of this disease. A sharply bordered, serpiginous lesion with lichenoid papules at the periphery could not be lupus erythematosus. This is the second patient with an unusual clinical type of sarcoid that Dr. Combes has presented. The other patient showed only a few reddish macules on the arm, yet the histologic picture was that of sarcoid.

DR. H. H. WHITEHOUSE: I agree that the condition is lichenoid sarcoid. The lichenoid papules at the periphery which Dr. Fox mentioned are, I think, particularly well shown in slanted light. That fairly well determines that the patient has lichenoid sarcoid. I did not see any features clinically resembling lupus erythematosus.

A CASE FOR DIAGNOSIS (MELANOSARCOMA?). Presented by DR. HANS J. SCHWARTZ.

K. W., a woman aged 60, a housewife, married, born in Russia, presents a pigmented lesion at the right side of the base of the nose, a "freckle," which has been present for four or five years and is now about 1 cm. in diameter. Within the area is a small growth of one half the diameter which started four months ago. This growth rises above the surface for about 0.5 cm. There is slight pigmentation on the base of the growth. The pigmented lesion is from dark brown to black, while the color of the tumor is that of a nonpigmented mole.

DISCUSSION

DR. GEORGE M. MACKEE: I agree with the diagnosis of melanoma. While such growths, as has been mentioned in connection with another case, vary markedly in the degree of malignancy, I think that this lesion should definitely be regarded as malignant and exceedingly dangerous. I favor some form of surgical intervention, such as electrosurgery or a plastic operation. Certainly the lesion should be removed. A good way to accomplish this is to give a very large dose of heavily filtered radium and then by electrosurgery to remove the entire lesion,

with a wide margin, down to the periosteum. Later, if necessary, the resulting defect can be repaired by a plastic operation. When radium is used in this way, of course, it is possible to give a much larger dose than ordinarily because the tissue is going to be removed. The lesion can also be removed by a plastic operation.

DR. HANS J. SCHWARTZ: I have nothing to add. The patient appeared for the first time at the clinic this afternoon, and I thought it would be of interest to get a clinical diagnosis. I am thoroughly in accord with Dr. MacKee's opinion as regards both diagnosis and treatment.

ACNE VARIOLIFORMIS OF ATYPICAL APPEARANCE. Presented by DR. PAUL E. BECHET.

This white woman, aged 29, states that the eruption began three months ago and has slowly increased since that time. She presents innumerable somewhat crusted, flattish lesions at the hair line of the forehead and over both temples, extending down to the cheeks. A number of them show necrotization at the center, and there is some indefinite, superficial pitting. The solid, rather large, violaceous red papule with definite central necrotization and varioliform scarring which is typical of acne varioliformis is absent. According to my experience, the eruption exhibited is not uncommon but differs greatly from typical acne necrotica. It may be that two types of this dermatosis exist, one similar to the eruption in this case, which quickly responds to local treatment, and another type more definitely related to the tuberculids and consequently more resistant to remedial measures.

DISCUSSION

DR. HOWARD FOX: The location is a favorite one for acne varioliformis, but the disease does not usually occur in females. Though a few lesions appear to have necrotic centers, many of them show punctate excoriations. The patient states that the eruption causes itching.

DR. H. H. WHITEHOUSE: This eruption does not present any features that suggest acne varioliformis to me. I agree with Dr. Fox. To have lesions like these is rather abhorrent to the patient, and her picking at them has changed their character. I do not think that the eruption is acne varioliformis. It seems to me that to a great extent it is due to traumatism.

DR. F. C. COMBES: I agree with what Dr. Whitehouse has said about the etiology. There is no inflammatory reaction. My conception of acne varioliformis is that the necrosis is secondary to an inflammatory reaction. These lesions are too superficial. They are covered with a very fine superficial crust, and I think that most of them have been produced by picking and trauma.

DR. E. F. TRAUB: I agree with the diagnosis as presented. The lesions present somewhat less inflammatory reaction than is usual in acne varioliformis, but I believe that such variations are not infrequently encountered. The woman is beyond the age at which acne ordinarily occurs. While some of the lesions have been scratched, the majority show no evidence of this, and I doubt that the uniform punctate scarring could have resulted largely from scratching.

DR. C. M. WILLIAMS: I think that the patient has folliculitis which has been aggravated by scratching.

DR. WALTER J. HIGHMAN: I think that the condition is acne varioliformis. I have seen this disease in women, although it is more often seen in men. I do not know of anything that could cause the degree of redness shown by these lesions except inflammation. As Dr. Fox said, the lesions may be exaggerated by the woman's scratching, but she certainly has something to scratch. I do not understand what Dr. Bechet meant in calling the condition a new entity. One cannot talk of a new entity until one has exhausted all the possible clinical variations of known diseases. This eruption is restricted to the forehead, tend-

ing to be most dense near the hair line and the temples, and consists of small inflamed papules which leave punched-out scars as they heal. If it is not acne varioliformis, I do not know what it can be.

Dr. George M. MacKee: I have seen a number of cases in the last few years in which the eruption was limited to the scalp and areas of the head close to the scalp, but the lesions were not typical of acne varioliformis; that is, they did not always occur in definite crops, necrosis was slight, and scarring was to a large extent absent, occurring only occasionally. Not being able to think of any better diagnosis, I have considered such cases to be instances of mild acne varioliformis, and I should place this case in that category until the condition is proved to be something else.

Dr. R. H. Rulison: I think that the patient has a low grade pyogenic infection with folliculitis. I do not agree as to the scars, except some which I saw that were due to an old acne. None of the lesions which Dr. Bechet pointed out suggested acne varioliformis to me. My impression of acne varioliformis is that the clinical diagnosis is usually made from the scars and not from the lesions. This patient has no scars, and I do not think that the condition is acne varioliformis.

Dr. Paul E. Bechet: I have frequently noted in the clinic cases similar to the one under discussion. The lesions in such cases are superficial. Some are crusted, some are slightly pustular and some show superficial necrotization. They occur in the typical sites of acne necrotica, but they are light red and the resultant scars are exceedingly light, if discernible. The clinical picture is therefore different from that of typical acne varioliformis, which presents deep red to violaceous red, inflamed papules, with marked central necrotization and resulting deep varioliform scars. I, of course, do not present this case with the idea that the condition is a new clinical entity, but I do believe that the clinical appearance taken as a whole is far from typical of acne varioliformis, and it may be a variant of that disease. It responds readily to local treatment, and that is not the case in typical acne varioliformis.

A Case for Diagnosis (Psoriasis?). Presented by Dr. Hans J. Schwartz.

This woman, aged 55, married, has no history of previous cutaneous disease. The family history is unimportant. There is a history of an injury to the right leg two years ago when the limb was struck against a ladder. The "bruise" healed, but three months later "blisters" appeared. One year ago the lesion had disappeared with the use of an ointment. About eight months ago, three or four blisters resembling "cold sores" appeared. These healed, and new ones appeared. Examination showed a circular, red, scaly lesion about 2 inches (5 cm.) in diameter about 3 inches (7 cm.) above the right ankle. Examination for tinea gave negative results. Examination of the urine for bromides revealed none. On Nov. 20, 1933, the report on examination of a biopsy specimen was as follows: "The histologic picture is not specific. There are some features of psoriasis, namely, parakeratosis, elongation of the papillae, etc. There is no histologic evidence of malignancy. The diagnosis is chronic inflammation." The patient received ¼ skin unit dose of roentgen rays (90 roentgens) on the following dates: September 28, October 5, 11, 18 and 25, November 8 and December 19.

DISCUSSION

Dr. J. Frank Fraser: I saw this patient at the New York Hospital. My associates and I were unable to make a diagnosis clinically. A section was removed, which I examined microscopically, and my report, which Dr. Schwartz read, suggests the diagnosis of psoriasis. Marked parakeratosis, decrease in the granular layer and papillae projecting almost up to the corneous layer strongly suggest psoriasis. I am not completely convinced that this eruption is psoriasis, but the histologic picture favors that diagnosis.

DR. FRED WISE: If I were to ignore the histologic observations, I should think of malignant disease or a precancerosis.

DR. WALTER J. HIGHMAN: Dr. Wise's impression is interesting. I think that if there were no other factors present in this case I should favor such a diagnosis. There is a definite history of injury to the lower part of the shin. If the leg is examined carefully, it will be found that the right leg is much thinner than the left, which is unusual. Moreover, the skin, not merely over the lesion but from about 3 inches (7 cm.) below the upper end of the tibia, cannot be picked up as easily as that on the left leg. I think that the condition is scleroderma. The ulcer itself does not look like scleroderma, but scleroderma when it has been injured leads to a type of lesion that is closely related to decubitus, and often a slough forms, as in this case. The lesion shows induration and does not discharge its contents easily and gradually sloughs a sequestrum as decubitus does. I think this is a case of decubitus on the basis of scleroderma.

DR. GEORGE M. MACKEE: I did not notice the features mentioned by Dr. Highman, but irrespective of whether the patient has scleroderma, I am inclined to regard the patch as psoriasis. The duration, which I understand is only a few months, is rather short for any form of malignant lesion, such as pagetoid keratosis or Bowen's disease, especially when one considers the large size of the lesion. Clinically one sees patches of psoriasis resembling this, that is, scaly at times, badly inflamed and even exudative. Finally, there is the histologic picture. There is no spongiosus to suggest eczema, nothing but the parakeratosis and the elongation of the papillae, as has already been mentioned, all of which is compatible with psoriasis.

DR. HOWARD FOX: I think that this is a patch of psoriasis clinically. It is not a great rarity for psoriasis to occur as a single patch. As stated by the presenter, the histologic picture at least suggests psoriasis.

DR. J. FRANK FRASER: Dr. Wise brought up the question of a clinical diagnosis of Bowen's disease. Bowen's disease was considered, but I could not find the slightest histologic evidence of that condition. Neither was there any evidence of any neoplastic process.

DR. WALTER J. HIGHMAN: I have listened with great interest to Dr. MacKee's remarks, and as I said before, if it were not for the rest of the picture, I should seriously consider a diagnosis of Paget's disease. However, I do not think that any of the speakers have taken into consideration the indolence of the ulcer, and I should like to know what picture Paget's disease presents when it is of four months' duration.

DR. HANS J. SCHWARTZ: The best diagnosis on the basis of the clinical picture and the histologic observations is psoriasis. As Dr. Fraser said, my associates and I suspected strongly that the patient had Bowen's disease, but that was excluded by the histologic examination. I have not seen any suggestion of sclerodermatous changes around the lesion, nor have I heard any of the men at the clinic mention such changes. I did not see or feel any sclerodermatous change tonight. I think that if there were any, it would show in a biopsy specimen taken from the skin near the red, scaly patch.

LYMPHOGRANULOMA INGUINALE (LYMPHOPATHIA VENEREA) TREATED WITH FREI VACCINE. Presented by DR. FRED WISE.

A. S., a man aged 28, born in Tampa, Fla., has been under the care of Dr. Silverberg and Dr. Sulzberger. The family history is irrelevant. He had gonorrhea without complications a year ago, and there is no history of syphilis.

On Sept. 13, 1933, he was operated on for hydrocele, the wound healing uneventfully, and was discharged from the Metropolitan Hospital on September 20. One or two days later, he noticed a swelling in the right inguinal region; this swelling increased in size, and the skin overlying it became purplish. This

was followed by the formation of discharging sinuses, which exuded a thick yellow pus during the next two months. The discharge gradually diminished. During the first week of his illness the patient had fever, dizziness and malaise.

Physical examination revealed adenopathy of the submaxillary, right axillary and epitrochlear glands and external and internal hemorrhoids. Examination of the rectum gave negative results. The right groin presented a well defined mass about 5½ by 4 inches (14 by 10 cm.). The skin over it was bound down and violaceous. The mass presented areas of induration and fluctuation, and the skin was indurated and puckered and bound down to the underlying tissues. There were three sinus openings, from which thick pus could be expressed.

The Wassermann and Kline tests were negative; the Kahn test was 1 plus. Examination of the aspirated pus for Bacillus tuberculosis, Ducrey's bacillus and gonococci gave negative results. Blood agar plates showed no growth. Repeated Frei vaccine tests with different antigens were positive, while tests with Dmelcos vaccine and graded tuberculin tests were negative. Roentgen examination of the lungs revealed nothing abnormal.

Biweekly injections of Frei vaccine (0.1 cc. intradermally) were administered. After the fourth injection, the patient had a mild fever and was sick for three days. Following that, there was definite improvement under this desensitization treatment (described by Wien and Perlstein: ARCH. DERMAT. & SYPH. **28**:42 [July] 1933), and the cutaneous reactions became successively weaker.

RESISTANT TERTIARY SYPHILIS WITH A NEGATIVE WASSERMANN REACTION. Presented by DR. C. M. WILLIAMS.

This Jewish woman, aged 60, has no personal or familial history of syphilis. The present condition began about two and one-half years ago with irritation in the nose and occasional hoarseness without known cause. About a year ago, the right cheek became swollen and hard, and a diagnosis of erysipelas was made. Later pustules appeared, as well as ulcers on the neck, trunk and extremities. In January, 1933, an experienced rhinologist examined the patient and suspected rhinoscleroma or tertiary syphilis. In spite of a negative Wassermann reaction, he started antisyphilitic treatment, but the patient did not return.

When I first saw her in June 1933, there was an ulcer on the left cheek; both cheeks and the nose were red and swollen, and the nares were crusted. There was extensive ulceration on the left side of the neck and the back, and smaller ulcers were present on both the upper and the lower extremities. The ulcers were shallow, with perpendicular edges, sometimes crusted. The left epitrochlear lymph nodes and the nodes in the neck and in the axillae were enlarged.

The patient was given 0.15 Gm. of neoarsphenamine, following which there was a rise of temperature to about 101 F. every evening. The Wassermann reaction forty-eight hours after the injection was negative. On account of the severe reaction to arsphenamine, she was given mercury for about ten weeks and showed great improvement in that time. Since the middle of August, she has received eight injections of neoarsphenamine, 0.45 Gm. each, two of a bismuth preparation and six of mild mercurous chloride. The ulcers have all healed, but a few pustules remain. She has used a 5 per cent ointment of ammoniated mercury locally and had nineteen general exposures to ultraviolet radiation.

SQUAMOUS CELL EPITHELIOMA OF THE CHIN? Presented by DR. E. F. TRAUB.

This man, aged 64, presents a lesion on the center of the chin which he states has been present for only six weeks. He is clear in his description of the onset, mentioning a small pimple which he cut while shaving. This failed to heal and continued to discharge a moderate amount of pus. The lesion has increased in size, reaching a diameter of 1.5 cm. Two or three weeks ago, a node became apparent in the submaxillary region, which continued to grow until it reached its present large size, from 2 to 3 cm. in diameter. The node seems to be com-

paratively soft with some slight fluctuation centrally. Repeated Wassermann tests have been negative. All bacteriologic studies, including examinations of numerous hairs for tinea and of pus for actinomycosis have given negative results. A section taken deep from the border of the lesion was reported on as follows: "The section shows a dense inflammatory exudate that extends deep into the tissue. The inflammatory exudate is covered by an acanthotic and hyperkeratotic epidermis. At one edge of the section there are numerous small islands of epithelial cells. The epithelial overgrowth has the appearance of hyperplasia associated with an inflammatory exudate rather than that of a neoplasm. No diagnosis can be made."

Although the microscopic examination made at the hospital did not confirm the tentative clinical diagnosis of squamous cell epithelioma, the negative results of bacteriologic examination and the negative Wassermann reaction lead me to believe that a diagnosis of squamous cell epithelioma is the most likely. On the other hand, the node under the chin is regarded as probably an inflammatory reaction rather than a malignant growth.

DISCUSSION

DR. J. FRANK FRASER: I agree with Dr. Traub's diagnosis of squamous cell epithelioma.

DR. WALTER J. HIGHMAN: Histologically the condition is squamous cell epithelioma, and I think that it resembles that condition clinically also.

DR. GEORGE M. MACKEE: Dr. Traub said that the large gland in the submaxillary region is soft. It seemed hard to me. This case is interesting because under the microscope the growth appears to be a squamous cell epithelioma but of a relatively low grade of malignancy. In spite of this and of the short duration, there is a large submaxillary gland. It is possible, of course, that the enlarged gland may represent inflammation rather than malignancy. While the lesion on the chin is probably an epithelioma, and I so regard it, mistakes are sometimes made in histologic examination when tissue is removed from the edge of an ulcer.

DR. E. F. TRAUB: I am sorry that the difference of opinion as to the diagnosis to be made from the section has resulted in some confusion. The pathologist refused to make a diagnosis of squamous cell epithelioma. Clinically it was felt that squamous cell epithelioma was the most likely diagnosis, largely on an exclusion basis. Assuming the lesion to be a squamous cell epithelioma, the question of the involvement of the submaxillary node is important and interesting. Recently I reported a series of twenty-six cases of squamous cell epithelioma of the glabrous skin, all confirmed by examination of tissue, and in only one of these cases was there an early involvement of a lymph node, occurring when the lesion had been present for only a few weeks. Excision of the lesion and the node in that case resulted in a cure, the patient having been followed for about five years. As none of the other cases in the series showed any metastasis I am of the opinion that in most instances squamous cell epithelioma does not metastasize early, although this differs somewhat from the impression given by Darier in reporting his series of cases.

DR. F. C. COMBES: Is there any history of a previous lesion or an injury?

DR. E. F. TRAUB: The man states that he had a small pimple on the chin from which pus discharged and that he cut this lesion while shaving.

DR. JOSEPH J. ELLER: I think that a primary lesion of syphilis should be considered. One would not expect an epithelioma to develop to this extent in six weeks or a large hard gland to develop in such a short time, especially with the microscopic picture described. I think that dark-field examination should be made and the blood test repeated.

DR. E. F. TRAUB: I do not believe that this node is hard enough to be carcinomatous. To answer Dr. Eller, six weeks' duration would be sufficient for the development of a squamous cell carcinoma to the size of this lesion. Such a tumor grows rapidly in the first three to six weeks, from which time on the growth is less rapid. This lesion has many of the clinical earmarks of a squamous

cell epithelioma, but it is not absolutely typical. The chief reason, however, for any doubt in the case was the reluctancy of the pathologist to make a diagnosis of epithelioma from the section. The biopsy was performed on a typical portion of the lesion, and a deep portion of the tissue was removed.

KERATOSES OF THE LOWER LIP. Presented by DR. E. F. TRAUB.

This man, aged 25, presents two lesions on the lip, the older one being of four months' duration. He has always complained of dry, chapped lips, but until the present trouble began his lips had always healed on the application of ointments. As one of the lesions has advanced far beyond the stage of ordinary keratosis, he is presented with the view of considering this an epithelioma and to obtain therapeutic suggestions.

DISCUSSION

DR. FRED WISE: I think that this lesion is an established carcinoma and should be removed.

DR. GEORGE M. MACKEE: I agree with Dr. Wise. The lesion has gone beyond the stage of keratosis and has become a carcinoma. My preference as to treatment, although excellent results can be obtained with radium or with electrosurgery, or with a combination, is a clean excision, preferably of one third of the lower lip.

DR. E. F. TRAUB: I was anxious to have an expression of opinion because of the two distinct lesions present. Do the members consider both of the lesions malignant or only one? One of the reasons for presenting the patient was that I have recently had two peculiar experiences with this type of case. In one instance I had a surgeon remove a large V-shaped wedge because of a similar lesion on the lip, and the tissue was reported to be nonmalignant. In the other case, one of much shorter duration in which the diagnosis of a malignant process seemed much less likely, the lesion was removed locally by electrosurgery and was reported to be a squamous cell epithelioma. Because the lesions in this case involve so large an area on the lower lip, I should not like to recommend a wide excision unless it seems absolutely necessary.

DR. GEORGE M. MACKEE: There is no contraindication, in my opinion, to taking a biopsy specimen.

DR. J. FRANK FRASER: I think that both lesions are probably malignant epithelioma.

CHANCROID (WITH A POSITIVE REENSTIERNA TEST). Presented by DR. HANS J. SCHWARTZ.

This man, aged 42, had intercourse four weeks and three weeks ago. A sore appeared on the penis one week later. It has seldom been painful. Inguinal adenitis developed a few days after the appearance of the sore. There is now a slightly indurated, eroded lesion the size of a dime on the left side of the foreskin anteriorly. The left inguinal glands are enlarged. Neither the penile lesion nor the inguinal glands are painful. There has been no cutaneous eruption. Dark-field examination of the penile sore and puncture of an inguinal gland on Dec. 15 and 16, 1933, gave negative results. The Kline exclusion and diagnostic tests on December 16 were negative. The Reenstierna test on December 16 produced a strongly positive reaction with an erythematous base 20 by 14 mm. and a central papule 9 by 9 mm. Five different antigens used in the Frei test on December 16 gave no reaction. There was no pus in the left inguinal glands.

ALOPECIA UNIVERSALIS WITH RETURN OF HAIR ON THE SCALP. Presented by DR. PAUL E. BECHET.

This white woman, aged 41, noticed a rapid loss of hair over the scalp and the hairy areas of the body in February, 1933. Within six weeks the hair had

disappeared, not even an eyelash remaining. Three months later hair began to return on the scalp, but nowhere else. She now has a thick growth on the scalp which is snow white whereas previously it was only slightly gray. Not a single hair has returned on the body. The case is of interest because of the prompt return of hair on the scalp, a most unusual occurrence in alopecia universalis, especially after the age of 40.

CLEVELAND DERMATOLOGICAL SOCIETY

J. R. DRIVER, M.D., *Reporter*

Regular Meeting, Dec. 21, 1933

SIDNEY LITTMAN, M.D., *Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. J. E. FISHER.

This white woman, aged 58, states that three weeks ago a sore developed on the right side of the upper lip which her family physician diagnosed as herpes simplex. The lesion did not follow the usual course of a herpetic process but refused to heal and became more extensive, with marked swelling of the upper lip and the right cheek. There is an area of sharply defined erythema almost the size of a palm on the right cheek, as well as marked enlargement of the submaxillary nodes, which are somewhat tender. The original lesion is approximately 2 cm. in diameter, is covered with a crust and extends onto the mucous membrane of the upper lip. On the adjacent surface of the mucous membrane of the lip there is a superficial ulcer about 1 cm. in diameter.

General physical examination revealed nothing abnormal. The white blood count during the past week has varied from 42,650 to 62,000. Differential blood counts have shown an average of 85 per cent small lymphocytes. The hemoglobin has been 80 per cent. The red blood cells have numbered 4,000,000. The Wassermann test of the blood was negative on two occasions and dark-field examination on two occasions did not disclose Spirochaeta pallida. Treatment has consisted of the application of hot compresses wet with saline solution and of soothing ointments.

DISCUSSION

DR. R. E. BARNEY: The appearance of the lesion, associated with the lymphadenitis, on first inspection resembles that of a primary lesion of syphilis. However, the blood picture is not consistent with this diagnosis, and for that reason I believe that the condition is identical with leukemic invasion of the skin as described in Jadassohn's "Handbuch der Haut- und Geschlechtskrankheiten."

DR. JOHN E. RAUSCHKOLB: The possibility of anthrax must be considered. The circular, crusted, necrotic area is fairly typical of this condition. The lymphadenitis also might be seen in anthrax.

DR. L. J. CARSON: I suggest that agglutination tests for tularemia be made.

DR. J. R. DRIVER: The area of erythema surrounding the crusted lesion clinically resembles erysipelas. The indurated, crusted lesion can be explained as ecthyma. The original lesion may have been herpetic, with a secondary streptococcic infection resulting in ecthyma and erysipelas. The adenopathy also is compatible with this diagnosis. Of course, this does not explain the preponderance of lymphocytes in the blood. The possibility of leukemia should, undoubtedly, be kept in mind.

DR. H. G. MISKJIAN: The theory of a pyogenic infection does not explain the finding of 85 per cent small lymphocytes. My impression is that the condition is leukemia.

DR. E. W. NETHERTON: I think that it is not uncommon for leukemic infiltrations of the skin to become secondarily infected and present the picture of a pyogenic infection. Perhaps that has happened in this case.

KERATODERMIA BLENNORRHAGICUM. Presented by DR. W. H. CONNOR.

This white man, aged 48, from the service of Dr. Cole and Dr. Driver at the Cleveland City Hospital, had gonorrhea in 1909, complicated by arthritis of the left knee and ankle. A similar attack of arthritis occurred in 1924. About two months ago a urethral discharge developed, with arthritis of both knees and ankles and of the right shoulder. Four weeks later, warty, crusted lesions appeared on the dorsa and soles of the feet, with a few scattered lesions on the legs.

There are now many large, pea-sized and smaller papules which are covered with crusts and contain a grumose, cheesy material. The tips of the toes show marked piled-up, keratotic lesions. There is extensive maceration in the interdigital areas. On the legs are similar crusted, rupioid papules. The left ankle, both knees, the right shoulder and the sternoclavicular joints are red, tender, swollen and painful. Smears made following prostatic massage showed many gram-negative intracellular diplococci. Cultures taken in an attempt to grow gonococci have as yet revealed none. The Wassermann test of the blood was negative.

DISCUSSION

DR. JOHN E. RAUSCHKOLB: The members will recall that several years ago Dr. Barrett was able to demonstrate the gonococcus in the cutaneous lesions in a case similar to this one (Barrett, C. C.: Keratoderma Blennorrhagicum, ARCH. DERMAT & SYPH. **22**:627 [Oct.] 1930). It will be interesting if the organism can be demonstrated in the lesions in this case and also if the gonococcus can be grown on the specific medium.

LYMPHOGRANULOMA INGUINALE. Presented by DR. W. H. CONNOR.

This Negro, aged 34, from the service of Dr. Cole and Dr. Driver at the Cleveland City Hospital, has had numerous exposures to infection through sexual intercourse. About one month ago he noticed a swelling of the left groin. After about three weeks the area broke down and discharged pus. There is no history of a recent penile lesion. There is now a large indurated mass in the left groin, with several discharging sinuses. On the surrounding skin of the thighs and abdomen there are scattered pustular, crusted lesions. There are several similar lesions on the forearms and on the fingers. The Wassermann test of the blood was negative. The Frei test was strongly positive.

LYMPHOGRANULOMA INGUINALE. Presented by DR. W. H. CONNOR.

This Negro, aged 33, from the service of Dr. Cole and Dr. Driver at the Cleveland City Hospital, had a bubo in the left groin in 1918, which subsided at the end of three weeks without treatment; in 1927 he had a similar lesion, which also subsided without treatment. There was no penile lesion in association with either of these infections. About four weeks ago the patient again noted an enlargement in the left groin. There is no penile lesion, and he denies having had extramarital intercourse. There is an area of firm, only slightly tender, matted adenitis about 3 inches (7 cm.) in diameter in the left inguinal region. The overlying skin is attached to the underlying mass and shows marked pigmentation. There is a purulent urethral discharge. The Wassermann reaction of the blood was 1 plus on one occasion and 2 plus at this examination. The Kline test of the blood was 4 plus on both occasions. The Frei test was strongly positive.

LYMPHOGRANULOMA INGUINALE. Presented by DR. W. H. CONNOR.

This Negro, aged 28, from the service of Dr. Cole and Dr. Driver at the Cleveland City Hospital, states that approximately four months ago, following

sexual exposure, a urethral discharge developed and that approximately two weeks later a small penile lesion appeared, followed by swelling in the groins. The lesion in the right groin broke down and was aspirated several times at the Lakeside Hospital. The patient was admitted to the City Hospital about three weeks ago. There is edematous phimosis, with a marked foul discharge. The left groin presents several discharging sinuses. The right groin shows marked adenitis with fluctuation. The nodes in this groin are matted together, and the overlying skin is firmly attached to the inflamed mass. The Wassermann test of the blood was 1 plus on one occasion and 3 plus on another. The Kline precipitation test was 4 plus on both occasions. The Frei test was strongly positive with two different antigens.

The patient has been receiving fuadin (a complex trivalent antimony compound), but no appreciable improvement has resulted.

LYMPHOGRANULOMA INGUINALE, ANORECTAL SYNDROME, ESTHIOMENE. Presented by DR. W. H. CONNOR.

This Negress, aged 29, from the service of Dr. Cole and Dr. Driver at the Cleveland City Hospital, shortly after her marriage in 1920 noted a vaginal discharge. In 1925, there developed marked swelling of both labia majora, the perineum and the perirectal regions. Repeated incisions with drainage were made, followed by healing. The condition recurred in 1929, associated with marked rectal stricture. In 1931, several perirectal sinuses and marked vulvar hypertrophy developed. The patient became weak and lost a great deal of weight, and when admitted to the hospital about eight weeks ago she was bedridden and had an irregular low grade fever. There are many sinuses about the vulva and perineum and in the perirectal region which discharge seropurulent material. The entire area is markedly indurated and shows chronic edema. There is a tube like stricture of the rectum, which admits a finger with difficulty. The Wassermann test of the blood in 1929 was reported as 3 plus. Several Wassermann tests made recently were 1 plus, 2 plus and negative. The Kline precipitation test of the blood has varied from 1 plus to 4 plus. The Frei test has repeatedly been strongly positive.

LYMPHOGRANULOMA INGUINALE, ANORECTAL SYNDROME, TERTIARY SYPHILIS. Presented by Dr. W. H. Connor.

This Negress, aged 47, from the service of Dr. Cole and Dr. Driver at the Cleveland City Hospital, six years ago noted a swelling of the vulva and perianal region. Discharging sinuses developed. There were periods of regression and exacerbation until the patient was admitted to the Cleveland City Hospital on Sept. 6, 1933. There are marked elephantiasis, chronic edema and multiple draining sinuses about the vulva and in the perianal regions. The entire area is markedly indurated. The pupils are fixed and do not react to light and in accommodation. The patellar reflexes are absent. The Wassermann test of the blood has been strongly positive on four occasions. The Wassermann test of the spinal fluid was strongly positive, and the fluid contained 33 cells and some globulin.

Antisyphilitic treatment consisting of the administration of bismuth and potassium iodide in addition to antimony and potassium tartrate and local treatments with filtered roentgen rays have been given. Surgical excision of the vulva has also been performed.

DISCUSSION ON CASES OF LYMPHOGRANULOMA INGUINALE

DR. H. N. COLE: This group of patients present several types of lymphogranuloma inguinale. The particular point that I should like to bring out is the variability of the Wassermann reaction in several of these cases. It will be noted that weakly positive reactions are not unusual and that they vary from time to time in the same patient. My associates and I have found that many patients

with this condition have a slightly positive reaction, which does not mean that they have syphilis, and this should be kept in mind. The first patient in this group had a pustular, crusted eruption which I am inclined to associate with lymphogranuloma inguinale. The literature contains reports of eruptions in patients with this disease. Surgical excision of the markedly hypertrophied labia in one case produced unusually good results, and a similar operation is contemplated for the other woman.

A Case for Diagnosis (Angiokeratoma or Multiple Angioma?). Presented by Dr. E. W. Netherton.

This white man, aged 25, had the usual diseases of childhood. Beginning at the age of 10 years, he had numerous attacks of a painful, tingling sensation in the toes and fingers. The attacks were associated with fever and occurred during warm weather. Relief from the pain could be effected by the application of cold compresses. The attacks of pain were always associated with marked perspiration of the hands and feet. At the age of 14, red areas the size of a pinpoint began to develop on the palmar surfaces of the hands, and similar lesions gradually appeared on the arms and legs during the following two years. These lesions presented no subjective symptoms. In the past few years these lesions have continued to develop, with involvement of the scrotum and penis.

General physical examination revealed nothing abnormal. On the palmar surfaces of the fingers and the extensor surfaces of the arms, especially in the regions of the elbows, and on the lateral surfaces of the thighs and over the buttocks there are numerous grouped, flat or raised, globular, lesions which vary in size from that of a pinhead to that of a match head and in color from light red to purple. The raised lesions are purplish, and the older, larger lesions feel keratotic. Over the scrotum, and to some extent on the penis, there are many small, slightly raised angiomatous lesions. Examination with the slit lamp revealed definite varicosities in many of the small capillaries of the conjunctiva. Ophthalmologic examination of the fundus showed a diffuse haziness of both disks. The Wassermann test of the blood was negative. The blood count and differential count were essentially normal. Biopsy performed on a specimen from one of the larger lesions showed marked thinning of the epidermis with slight hyperkeratosis. In the papillary layer were two large cavernous sinuses filled with blood, resulting in the thinning of the superficial layers. There was a slight inflammatory reaction surrounding the cavernous areas. No pathologic changes were noted in the corium.

No treatment has been given.

DISCUSSION

Dr. H. G. Miskjian: The question to decide is: Is the condition angiokeratoma? It certainly is not the type described by Mibelli. I do not know whether cases of Mibelli's angiokeratoma have been observed in which the lesions were spread over as large areas as in this case. But the lesions on the scrotum are small angiomas with horny tops. They deserve, therefore, the name of angiokeratoma. The lesions on the thighs and elsewhere are also angiomas, but many of them are not raised, and their surfaces are not horny. The lesion on the thigh on which biopsy was performed could be considered a typical angiokeratoma if the hyperkeratosis were more marked. If the biopsy specimen had been taken from the scrotum, I have no doubt that considerable hyperkeratosis would have been observed. The condition may be looked on either as angiokeratoma in which the elements on the trunk and limbs have not yet acquired the horny tops characteristic of that syndrome or as a transitional type between angiokeratoma and multiple angioma. Can one not conceive of Mibelli's angiokeratoma as a special variety of multiple verrucous angioma?

Dr. E. W. Netherton: Before presenting the patient I looked up some of the literature on angiokeratoma. In 1928, Dr. Wile reported a case of angiokeratoma with a subtitle, representing a much confused clinical entity. In his

article he showed that angiomas on the scrotum, which are seen often, as well as the senile angiomas, which are similar in type, should not be considered as angiokeratoma. The clinical picture in the case now under discussion fits in well with the descriptions of angiokeratoma that appear in some textbooks. The lesions on the arms and legs are not as bright red as ordinary senile angiomas. They vary from the size of a pinhead to that of a match head. Many are slightly elevated and give the impression of being hyperkeratotic crusts. Some look as if they contained coagulated blood. Hyperkeratosis cannot be made out clinically; however, histologically there is some hyperkeratosis. A slight inflammatory reaction was observed in the biopsy specimens. In Dr. Wile's case the sections showed a marked inflammatory reaction in the dermis and some hemorrhages. There is no history of chilblain in the present case. The man is young, and consequently one would not expect senile angioma.

An unusual feature is the terrific pain in the hands and arms, which is brought on by heat. In the hot weather it becomes excruciating, and the patient can hardly tolerate contact with clothing or bedding. He states that the skin becomes somewhat flushed during these attacks. I have not observed this reaction. There are no abnormal neurologic findings. My associates and I have felt that the condition is probably erythromelalgia.

So far I have been unable to classify this case definitely, but I do not feel that the lesions are simple angiomas.

BRONX DERMATOLOGICAL SOCIETY

HENRY SILVER, M.D., *Secretary*

Regular Meeting, Dec. 28, 1933

SAMUEL FELDMAN, M.D., *President*

MANIFESTATIONS ON THE MUCOUS MEMBRANES IN A CASE OF LYMPHATIC LEUKEMIA. Presented by DR. SAMUEL FELDMAN.

This white woman, aged 28, entered the Morrisania City Hospital on Dec. 6, 1933, with chief complaints of weakness, cough and pain in the arms and shoulders for the past three weeks. She was pregnant.

Physical examination on admission revealed signs of six months' pregnancy, marked anemia and a tendency to hemorrhages of the gums. The parotid glands were enlarged and tender. The eyegrounds contained flame-shaped hemorrhages.

The mouth showed several shallow, oval ulcers surrounded by a whitish border on both buccal mucous membranes. The ulcers were tender and bled easily. There was definite infiltration of both lips, and tenderness was noted on the slightest motion.

The blood picture during her stay in the hospital was as follows:

	White Cells	Red Cells
12/ 7/33	70,000	2,160,000
12/13/33	128,000	1,880,000
12/17/33	78,000	3,040,000
12/20/33	39,500	.....
12/26/33	24,800	.....

On December 7, the patient received a transfusion of 500 cc. of blood. On December 8, labor was induced, by means of a bag. On December 9, the patient was delivered of a stillborn infant. Her temperature rose to 103 F. On December 12, she received a transfusion of 500 cc. of blood, and on December 20, another transfusion of 500 cc.

The patient's condition is now greatly improved. She has recovered her appetite and feels stronger. The blood count is approaching normal, and the lesions in the mouth have almost entirely cleared. This may be one of the rare cases of leukemia incited by pregnancy and relieved by delivery.

DISCUSSION

DR. S. FELDMAN: It has been demonstrated that lymphatic leukemia occurring during pregnancy is often improved by blood transfusions. This patient responded well to this form of treatment, as evidenced by the involution of the lesions in the mouth and the changes in the blood picture approaching the normal.

XANTHOMA TUBEROSUM MULTIPLEX. Presented by DR. SAMUEL FELDMAN.

This white woman, aged 55, states that the first lesions appeared on the elbows twelve years ago. They soon increased in number and spread to the trunk, extremities, back and ischiospinal region. Two years ago she noticed involvement of the eyelids. The lesions are located on areas over and around the joints, including the dorsal and palmar surfaces over the phalangeal joints and the cubital and popliteal fossae. Several of them are confluent and form lobulated tumors. The smaller lesions are yellow, while the larger ones vary from bluish to reddish yellow. They vary in size from that of a pea to that of a small egg and are freely movable in the skin. Some of the lesions contain calcified infiltrations.

In addition, the patient presents xanthoma planum of the eyelids. These lesions are flat and slightly elevated and of a lighter yellowish color.

The patient has not shown any signs or symptoms of diabetes during the many years that she has been going to clinics for the treatment of her cutaneous condition. She has chronic cardiac hypertension.

The blood cholesterol was 207.5 mg. per hundred cubic centimeters. The blood sugar was 83 mg. The urine contained no sugar. Roentgen examination of the skull and lungs showed no abnormality.

Histologic study revealed the cutis to be infiltrated with large, oval, round and polyhedral cells, very lightly stained and appearing foamy or vacuolated. Slides stained with sudan III show the protoplasm to consist of a fatlike substance in the form of small droplets and granules which take a positive stain for fat.

DISCUSSION

DR. H. SILVER: Such generalized cases of xanthoma with oversized tumors are rarely seen. The finding of hypercholesteremia is not essential. It is important, though, to estimate the ratio between the free cholesterol and the cholesterol esters. In an extensive case of xanthoma tuberosum of many years' duration I found a normal amount of cholesterol in the blood, but the ratio was disturbed. In my case the marked involvement of the face and neck was somewhat unusual. It is of interest that the patient died of lymphatic leukemia showing a typical blood picture.

A SOLITARY LESION ON THE CHEEK OF A CHILD WITH CONGENITAL SYPHILIS. Presented by DR. MAURICE UMANSKY.

This girl, aged 26 months, born in Cuba, for five or six months has had an ulcerated lesion on the cheek. The Wassermann test of the blood was 4 plus. Both parents also gave positive Wassermann reactions. The child presents no stigmas of congenital syphilis. She has a geographic tongue.

There is an oval, sharply demarcated, bluish-red lesion the size of a silver quarter on the right cheek. It shows scarring in the center and signs of activity at the periphery. The border is edematous and slightly raised. Fine yellowish-

brown points can be seen through a glass slide in the center and at the border. The lesion has improved somewhat under bismuth therapy.

The Pirquet test was negative; the Mantoux test with dilutions of 1:1,000 and 1:10,000 was positive.

DISCUSSION

DR. E. BERNSTEIN (by invitation): In Moscow I observed several cases of congenital syphilis with solitary ulcers. This appears to be a case of that type.

DR. I. M. LASHINSKY: Although one must consider gumma, especially in view of the response to bismuth therapy, tuberculosis cannot be ruled out on clinical grounds. The histologic structure may be similar in the two diseases.

DR. C. LERNER: I do not think that the pathologic pictures in tuberculosis and syphilis are so much alike. In tuberculosis cutis there are tubercles, epithelioid cells and giant cells. One rarely finds giant cells in syphilis.

DR. W. SACHS: The histologic pictures in some cases of tuberculosis and syphilis cannot be differentiated, but it is worth remembering that in tuberculosis there is granulation tissue whereas the lesion of syphilis is a granuloma.

DR. M. UMANSKY: If the lesion were tuberculous the healing would not have been so rapid with bismuth therapy; hence I believe it to be a gumma.

ACRODERMATITIS CHRONICA ATROPHICANS WITH HEALED ULCERATIONS. Presented by DR. ISADOR LASHINSKY.

R. H., a widow, 58 years of age, an Austrian Jewess, came to the clinic on Oct. 3, 1933, for treatment of ulcerations of both legs which had developed ten months previously. The past history was unimportant. She had given birth to five children, who were living and healthy. She said that for the past ten months she had had to spend most of the time in bed on account of itching, painful swelling of the legs and the ulcers.

On admission she presented somewhat irregular, deep-seated ulcerations varying in size from that of a walnut to that of an egg, extending from the middle third of the legs to the ankles. The legs appeared violaceous and shiny, and the skin was markedly thinned so that the underlying veins were plainly visible. There were impetiginous lesions caused by scratching, and the ulcers were infected.

Physical examination revealed nothing significant. The urine was normal, and the Wassermann test of the blood was negative. The application of wet dressings for a time and absolute rest in bed helped to clear the ulcers. The legs were then bandaged with an adhesive elastic bandage (elastoplast), and the bandages were kept on for one week. On their removal the ulcers were markedly improved. Bandages were again applied. The ulcers have practically healed, and the patient attends to her work.

DISCUSSION

DR. F. CROSS: In addition to the acrodermatitis there are varicose veins of long standing, and because of this I think that the immobilization has aided the general condition. I suggest injection therapy of the veins.

DR. R. BREAKSTONE: One rarely sees ulcerations in acrodermatitis; therefore, the varicose veins may be a contributing factor. Because of the age of the patient I should hesitate to make injections into the veins.

DR. E. BERNSTEIN: I have seen sixteen cases of acrodermatitis chronica atrophicans in the Herxheimer Clinic. Cases with ulcerations were rare, but cases presenting scleroderma were found.

DR. H. SILVER: The disease seems to be more frequent in this country. Dr. Cross' impression that the veins shining through the thinned and atrophic skin are varicose veins I believe to be erroneous.

DR. S. FELDMAN: The improvement in this case is remarkable. It would be dangerous to make injections into the varicose veins.

SECONDARY MACULAR ATROPHY FOLLOWING SYPHILIS (ATROPHIA MACULOSA SYPHILITICA). Presented by DR. HENRY SILVER for DR. THEODORE ROSENTHAL.

R. M., a colored man, aged 42, born in the United States, in 1918, had a primary syphilitic lesion, which was followed by a generalized eruption. Several years later he noticed peculiar spots on the body. He was first treated in 1923. He is under treatment at present at the Harlem Hospital. Physical examination disclosed an enlarged heart and aortic regurgitation.

The patient presents on the back, shoulders and anterior thoracic region a number of oval or round, depressed or elevated lesions, varying from 1 to 2 mm. in diameter. Many lesions follow the lines of cleavage. Most of the lesions are elevated and bullous-like and have wrinkled surfaces

DISCUSSION

DR. F. CROSS: Do the atrophic spots conform in size with the primary syphilitic papules? Some of the spots appeared considerably larger than the usual syphilitic papules.

DR. I. M. LASHINSKY: Does such atrophy follow only papular eruptions? It would be interesting to know whether malignant or pustular syphilis produces it.

DR. H. SILVER: The preceding syphilitic lesion has apparently nothing to do with the size of the atrophic spot. The replacement does not seem to be due to direct spirochetal action, which can be explained on the basis that the spirochetes have no affinity for the elastic tissue.

A syphilitic eruption does not have to be severe to produce secondary atrophy. Moreover, the type of the eruption is of no importance. Atrophy has been observed following macular and papular eruptions and even tertiary lesions.

The apparent discrepancy between the frequent occurrence of syphilis and the comparatively rare occurrence of secondary macular atrophy requires an explanation.

NOTE.—We assume a weakened resistance of the elastic tissue in certain persons. These persons seem to furnish a fertile soil for the attack of the syphilitic infection probably by way of the endocrine or sympathetic nervous system.

FIXED ERUPTION FOLLOWING THE ADMINISTRATION OF ARSPHENAMINE. Presented by DR. HENRY SILVER for DR. THEODORE ROSENTHAL.

G. C., a colored man aged 47, born in the United States, had an initial lesion one and one-half years ago. Treatment with arsphenamine was begun three months ago. During the course of treatment he noticed black spots on the body which increased in number.

He now presents a number of irregular, dark brown to black, macular, pigmented areas, ranging from 1 to 4 cm. in diameter, distributed over the arms, hips and face. There are no subjective symptoms.

Book Reviews

The Dermatergoses or Occupational Affections of the Skin. By R. Prosser White. Fourth edition. Price, 35 shillings, net. Pp. 716, with 66 plates. London: H. K. Lewis & Co., Ltd., 1934.

The fourth edition of White's "Occupational Affections of the Skin" has just been published, and any one who knows of his interest and indefatigable industry in this field of medicine need not be told that it has been brought up to date. It covers the whole field as no other work in English does. In order to do this, in this edition, as in the second and third, the author recast almost the entire text and made a new volume. To cover the whole field without increasing the extent of the text, he condensed the subject as far as possible, but every subject is considered, though often concisely. One wishes that he had not felt himself so restricted in space and had given his unequaled knowledge in this field freer range. Often when there is a brief statement with reference to the literature, those who know the fulness of White's knowledge and the way in which his interest was aroused by his subject can only wish that he had given himself the opportunity for fuller expression. The book is invaluable. It is a classic in its field, and may in time rank with Ramazzini's "De morbis artificum diatriba."

The fourth edition is the last edition of this work that White will produce; the final proofs were read by him only two days before his fatal seizure, and he wrote that he would return them personally the following week. The work was finished by White himself.

"To a reader a book is a tool to use, a tilt to abuse, or a toy to amuse: but mirrors the soul of the writer." This inscription was placed by White at the beginning of the book. It accurately describes White's work; it mirrors the soul of the writer and is a fine monument to him.

Tuberculose cutanée et tuberculides. By J. Nicolas and J. Gaté. Price, 80 francs. Pp. 482, with 74 illustrations. Paris: Gaston Doin & Cie, 1934.

This volume of nearly 500 pages is devoted to a consideration of tuberculosis of the skin and the tuberculids. It is an excellent presentation of the subject, well illustrated, and could hardly be produced in this country, where, thank Heaven, physicians have no such large experience in cutaneous tuberculosis as have physicians in most of the countries in Europe. Every aspect of the field is fully covered. In the introduction of twenty-four pages every phase of the subject of the tubercle bacillus is considered. In part 1, of forty-three pages, the general features of cutaneous tuberculosis and the tuberculids, including their pathologic aspects, are presented. In part 2, of 130 pages, the anatomic and clinical forms of cutaneous tuberculosis are considered in detail. In part 3, of 125 pages, the authors take up the various tuberculids in the same detail that is given to tuberculosis of the skin in the preceding part. Then, after a consideration of the various dermatoses which are suspected of having a relationship to tuberculosis and after a discussion of the general diagnosis and prognosis of cutaneous tuberculosis and the tuberculids, comes part 7, of almost 100 pages, which is a clear and full exposition of the whole subject of therapeutics, both of cutaneous tuberculosis and of tuberculids.

The work is a complete and authoritative presentation of the subject and is a credit to its distinguished authors. It would be fortunate if there could be an English translation.

A Practical Treatise on Diseases of the Skin. By Oliver S. Ormsby and Clark Wylie Finnerud. Price, $11.50. Pp. 1,288, with 622 illustrations. Philadelphia: Lea & Febiger, 1934.

The fourth edition of Ormsby's "Practical Treatise on Diseases of the Skin" is a handsome book of 1,288 pages, with 622 illustrations. Ormsby has found it necessary to describe 36 new syndromes, and this is no imaginary necessity. With the opportunity for accurate observation that diseases of the skin afford, new syndromes are constantly determined, and these must be described. Dermatology is in a way the author's religion, and this is reflected in the work. The accuracy of his knowledge and the meticulous quality of his expositions are a reflex of the man. Everything is brought up to date, and everything is considered. The histopathology of the various diseases described in this edition has been revised by Finnerud. He also is conscientious and accurate in his knowledge and gives an authoritative statement of the various pathologic pictures. The work is handsomely gotten up. The illustrations are well selected, of high quality and beautifully reproduced and are sufficient in number to illustrate most of the subjects and various aspects of many of the more important ones. A book that has gone through four editions, as this has done, does not require any commendation; its success is established on its record.

Fisiologia normale e patologica della cute umana. By M. Comel. Vol. 1, 971 pages; Vol. II, 675 pages. Milan: Fratelli Treves, Editori, 1933.

These two large volumes on the normal and pathologic physiology of the human skin, aggregating more than 1,600 pages, are a monument to the scientific achievement and scholarship of Dr. M. Comel, docent in dermatology at the University of Milan. Pasini, director of the dermatologic clinic at the University of Milan, appropriately furnishes a preface to the volumes, in which he, with justice, expatiates on the extensive and excellent presentation of this field which Dr. Comel has given.

Of course, in a work so complete every phase of the subject is covered. The elaborate presentation of the chemical physiology of the skin should be noted particularly. The work is one which cannot be overlooked in a thorough consideration of any topic in cutaneous physiology. Such a work reminds one again of the vast handicap to civilization which results from a multiplicity of languages among the educated. But, fortunately, the author's style is so clear and simple that the reading of his Italian is relatively easy even for a novice. The work is a magnificent achievement.

Handbuch der Haut- und Geschlechtskrankheiten. Edited by J. Jadassohn. Volume II. Price, 108 marks; bound, 116 marks. Pp. 507, with 236 illustrations. Berlin: Julius Springer, 1932.

This is volume II of this distinguished encyclopedia many other volumes of which have been reviewed in this journal. It is rather curious that the volumes should be presented in such an irregular order, but this is about the only criticism to be made of them.

In this volume the diseases of the skin due to protozoa and filtrable viruses and the manifestations in the skin of the reactions of immunity are considered. These subjects take one into an important group of dermatoses, of which the eruptions of smallpox and vaccinia are typical, and into another group of less important but none the less interesting and curious lesions, such as molluscum contagiosum and verrucae. As usual in this series, the subjects are considered with great fulness and in detail, and the authors are among the familiar German dermatologists. The volume comes up to the high standard of excellence which has been praised so frequently in reviews of the preceding volumes.

Directory of Dermatologic Societies *

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

W. R. Jaffrey, President, 64 Hughson St., S., Hamilton, Ont.
Basil Bowman, Secretary-Treasurer, 408 Medical Arts Bldg., Hamilton, Ont.
Place: Hamilton, Ontario. Time: 1934.

Royal Society of Medicine, Section of Dermatology

Henry MacCormac, President, 23, Wimpole St., W. 1, London.
W. N. Goldsmith, Secretary, 6, Upper Wimpole St., W. 1, London.

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

C. Guy Lane, Chairman, 416 Marlboro St., Boston.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.

American Dermatological Association

Harold N. Cole, President, 1422 Euclid Ave., Cleveland.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Harry F. Anderson, President, 1610, 20th St. N.W., Washington, D. C.
Joseph V. Kennedy, Secretary, 1835 Eye St., Washington, D. C.

Central States Dermatological Association

Joseph Brumberg, President, 528 Delaware Ave., Buffalo.
William F. Hoover, Secretary, 333 Linwood Ave., Buffalo.
Place: Buffalo. Time: 1934.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City.
Robert E. Jameson, Secretary, 1014 First National Bank Bldg., Davenport, Iowa.

New England Dermatological Society

Rudolph Jacoby, President, 270 Commonwealth Ave., Boston.
J. Harper Blaisdell, Secretary, 5 Bay State Road, Boston.

Southern Medical Association, Section on Dermatology and Syphilology

Thomas W. Murrell, Chairman, 17 E. Grace St., Richmond, Va.
C. C. Dennie, Secretary, Professional Bldg., Kansas City, Mo.
Place: San Antonio, Texas. Time: November, 1934.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
Elmo D. French, Secretary, 602 Huntington Bldg., Miami.
Place: Jacksonville. Time: July 2, 1934.

Louisiana Dermatological Society

J. A. Devron, President, 150 Baronne St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 912 Pere Marquette Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

George M. Fisher, Chairman, 264 Genesee St., Utica.
Frank Combes, Secretary, 80 W. 40th St., New York.

Medical Society of the State of Pennsylvania Section on Dermatology

Herbert J. Smith, President, 3303 N. 17th St., Philadelphia.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Michigan State Medical Society, Section on Dermatology and Syphilology

Robert C. Jamieson, Chairman, 1551 Woodward Ave., Detroit.
A. R. Woodburne, Secretary, Grand Rapids Clinic, Grand Rapids.
Place: Battle Creek. Time: September, 1934.

Minnesota Dermatological Society

D. D. Turnacliff, President, 407 Medical Arts Bldg., Minneapolis.
L. H. Winer, Secretary, 522 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

Oklahoma Dermatological Association

W. A. Showman, President, 108 W. 6th St., Tulsa.
C. L. Brundage, Secretary, 505 Osler Bldg., Oklahoma City.

Texas Dermatological Society

C. F. Lehmann, President, 303 E. Houston St., San Antonio.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Louis Chargin, Chairman, 1 W. 85th St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

Brooklyn Dermatological Society

Arthur Persky, President, 1750 Ocean Parkway, Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo-Rochester Dermatological Society

Earl D. Osborne, President, 471 Delaware Ave., Buffalo.
Richard L. Saunders, Secretary, 33 Linwood Ave., Buffalo.

Chicago Dermatological Society

James H. Mitchell, President, 25 E. Washington St., Chicago.
Max S. Wien, Secretary, 104 S. Michigan Ave., Chicago.

Cincinnati Dermatological Society

Harry L. Claassen, President, Provident Bank Bldg., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

R. E. Barney, President, 1021 Prospect Ave., Cleveland.
E. W. Netherton, Secretary, 2020 E. 93d St., Cleveland.

Detroit Dermatological Society

H. L. Keim, President, 10 Witherell St., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

Moses Scholtz, Chairman, 1930 Wilshire Blvd., Los Angeles.
Nelson P. Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles.

Manhattan Dermatologic Society

Louis B. Mount, Chairman, 256 State St., Albany, N. Y.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

J. F. Burgess, President, Drummond Medical Bldg., Montreal, Canada.
B. Usher, Secretary-Treasurer, 1538 Sherbrooke St., W., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Ray H. Rulison, Chairman, 145 E. 54th St., New York.
E. William Abramowitz, Secretary, 853, 7th Ave., New York.

New York Dermatological Society

Edward R. Maloney, President, 853 7th Ave., New York.
R. H. Rulison, Secretary, 145 E. 54th St., New York.

Omaha Dermatological Society

J. W. Hellwig, Chairman, 1319 Farnam St., Omaha.
Donald J. Wilson, Secretary, 1216 Medical Arts Bldg., Omaha.

Philadelphia Dermatological Society

Robert L. Gilman, Chairman, 1930 Chestnut St., Philadelphia.
Vaughn C. Garner, Secretary, Greene and Coulter Sts., Philadelphia.

Pittsburgh Dermatological Society

Frederick Amshel, Chairman, 3401 5th Ave., Pittsburgh.
Bernhard Goldmann, Secretary, Jenkins's Arcade, Pittsburgh.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

H. J. Templeton, President, 3115 Webster St., Oakland, Calif.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

INDEX TO VOLUME 29

The asterisk (*) preceding the page number indicates an original article. Subject entries are made for all articles. Author entries are made for original articles, correspondence and society transactions. Biographies, Book Reviews, Obituaries and Society Transactions are indexed under these headings in their alphabetical order under the letters B, O and S, respectively.

Acanthosis nigricans, case of benign form in adult investigated from aspect of endocrine dysfunction, *691
nigricans, familial juvenile, 728
nigricans, juvenile benign form, 763
nigricans; tertiary syphilis; scirrhous carcinoma of stomach (inoperable), 942
Acetarsone Therapy: See Lichen planus; Syphilis, congenital
Achromia: See Pigmentation
Acid, chlorosulphonic acid cauterization as industrial accident, 115
Acid-Base Equilibrium; relation between an acid or an alkaline diet and immunity, 431
Acne in 1 of identical twins, *706
indurata of unusually severe type, 633
rosacea treated with alkaline sulphur ointment, 612
varioliformis of atypical appearance, 956
vulgaris and roentgen radiation, 116
Acrodermatitis chronica atrophicans, 126
chronica atrophicans with healed ulcerations, 968
chronica atrophicans with sclerodermatous changes, 731
Acrodynia, 309, 428
etiology and treatment of pink disease, 309
juvenile, 783
Acromegaly in form of cutis verticis gyrata, 164
Acrostalagmus cinnabarinus: See Trichophytosis
Actinomycosis without granules, *287
Adenitis: See under Lymph Nodes
Adenoma sebaceum, 139
sebaceum, Balzer's type, 738
sebaceum, familial, 472
sebaceum, identity of adenoma sebaceum, neurofibromatosis and subungual fibromatosis, 116
sebaceum with tuberous sclerosis, 920
Advisory Board for Medical Specialties, 899
Agranulocytosis: See Angina, agranulocytic
Alcoholism, etiologic relationship of alcoholism to pellagra, 428, 441
pellagra secondary to, 444
pseudopellagra due to alcohol, 635
Alderson, H. E.: Morphea, 436
Allergy: See Anaphylaxis and Allergy
Allington, H. V.: Sulpharsphenamine in treatment of warts, *687
Alopecia areata and lichen planus in child, 131
areata, pathogenesis, 722
pseudopelade with unusual manifestations or folliculitis decalvans, 461
universalis with return of hair on scalp, 961
Ambler, J. V.: Porokeratosis (Mibelli); its occurrence in Negro, *20
American Board of Dermatology and Syphilology, examinations for certificates, 105, 307
step forward in supervision of specialism, *1
American Medical Association, Cleveland Session, Scientific Exhibit, 105
Amidopyrine, pustular exanthem resembling smallpox due to melubrin, 115
Amshel, F.: Familial telangiectasia, 778
Mycosis fungoides, 783
Scleredema, 777
Amyloidosis of skin, 470, 911
systematized, of skin and muscles, *805
Anaphylaxis and Allergy; cutaneous manifestations of allergy, *333
mechanism of urticarial idiosyncrasy to egg white in eczematous child, 912
persistence of immunity after abolition of allergy by desensitization, 431
rattlesnake anaphylaxis associated with generalized dermatitis, *658
results of intradermal tests with various vaccines using measured amounts of nitrogen, 935
sensitization tests, their value in dermatology, *845
transferable and inhibiting substances in blood of allergic patients, 433
Anderson, N. P.: Acne rosacea treated with alkaline sulphur ointment, 612
Adenoma sebaceum with tuberous sclerosis, 920
Case for diagnosis, 923
Granuloma annulare, 613
Inhibition of fungi in cultures by blood serum from patients with "phytid" eruptions, *537
Lupus erythematosus in child, 927
Lupus pernio, 732
Recklinghausen's disease, 924
Andrews, G. B.: Nevus unilateralis or linear lichen planus, 454
Andrews, G. C.: Bowen's precancerous dermatosis, 934
Keloid, 933
Pustular eruption of palms and soles, 741
Recalcitrant pustular eruptions of palms and soles, *548
Anemia, splenic; syphilitic tumor of spleen associated with symptom complex of Banti, 727
Anetodermia: See Atrophy
Angina, agranulocytic, in childhood, 428
Angiokeratoma or multiple angioma, 965
Angiolupoid or tertiary syphilis, 439
Angioma, generalized angiomatosis (telangiectasia), 907
or angiokeratoma, 965
Angioneuromyoma, rare tumors of nail bed (neuromyo-arterial glomus tumors or arterial angioneuromyoma), 118
Anthrax, human, effective treatment with organic arsenic preparations, 909
Anus, genito-ano-rectal lymphogranulomatosis of male, 722
Aortitis, syphilitic, uncomplicated; diagnosis, prognosis and treatment, 607
Apparatus, use of filiform douche in dermatology and advantage of new apparatus, 116
Appel, B.: Pityriasis lichenoides et varioliformis acuta (Haberman), 948
Psoriasis; dermatophytosis; keratosis blennorrhagica, 319
Argyria; Argyrosis: See under Silver
Arsenic, chronic ulceration of soles (Bowen's disease); multiple benign superficial epitheliomas; arsenical keratoses (palms, soles, trunk), 613
dermatitis (lichenoid type), 919
in etiology of acrodynia, 309
in tissues; methods for microchemical demonstration, 430
optic nerve and pentavalent arsenicals, 909
Arsphenamine: See also under Syphilis
combined action of arsphenamine and ultraviolet rays on Spirochaeta pallida, 432
dermatitis, 122
dermatitis, intradermal tests in relation to study based on 256 clinical cases, *485

Arsphenamine—Continued
dermatitis; treatment of postarsphenamine dermatitis, *173
fixed eruption following administration of arsphenamine, 969
hemorrhage and impairment of blood after, 314
leukomelanoderma due to injury of vegetative nervous system caused by, 435
pathogenesis of cutaneous reactions to arsphenamine and their prevention, 725
serum albumin in its relations to dermatology; influence of arsphenamine on serum albumin in syphilis in man and in experimental rabbits, 434
Asthma, ioderma from asthma remedy (Felsol), 905
Ataxia: See Tabes
Atrophoderma: See Atrophy
Atrophy; anetodermia maculosa, 327
atrophoderma and keloidal scars following erythema multiforme, 798
atrophoderma with telangiectasia, 157
cutis maculosa, 919
dermatitis atrophicans progressiva; dermatochalasis (flabby skin) with attention to its pathogenesis and relationship to dermatitis atrophicans progressiva, 116
idiopathic macular atrophy, 112
idiopathic, with poikiloderma-like changes, 156
macular (anetodermia of Schweninger and Buzzi), 133
macular, in congenital syphilis, 776
macular; multiple benign tumor-like new growth of Schweninger-Buzzi type; reports of case, *219
pseudo-atrophoderma colli: hitherto undescribed condition, *53
secondary macular atrophy following syphilis (atrophia maculosa syphilitica), 969
syphiloderm (late extensive) with atrophy and juxta-articular nodes, 775
vermiform cutaneous atrophy, 911
Avitaminosis: See under Vitamins
Ayres, S., Jr.: Acrodermatitis chronica atrophicans with sclerodermatous changes, 731
Actinic dermatitis with lesions resembling hydroa aestivale on face and prurigo aestivale on arms, 926
Chronic ulceration of soles (Bowen's disease); multiple benign superficial epitheliomas; arsenical keratoses (palms, soles, trunk), 613
Inhibition of fungi in cultures by blood serum from patients with "phytid" eruptions, *537
Lichen spinulosus, 733
Ulceration of unknown origin, 732
Urticaria pigmentosa, 732

Bacillus Ducrey; infection with Ducrey bacillus with eczematous eruption, 954
Bailey, R.: Cutaneous reactions with purified oidiomycin, *564
Bakers' itch, cause of industrial eczema in bakers, clinical and animal experiments, 724
pathogenesis, 314
Baldness: See Alopecia
Banti's Disease: See Anemia, splenic
Barrett, C. C.: Acute interstitial myocarditis; report of case following severe dermatitis due to sulphur ointment, *382
Bechet, P. E.: Acne indurata of unusually severe type, 633
Acne varioliformis of atypical appearance, 956
Alopecia universalis with return of hair on scalp, 961
Dermatosis papulosa nigra, 753
Excessive solar and phototherapeutic irradiation; causative factor in certain diseases of skin, *221
Extensive lupus erythematosus, 764
Iodized table salt as etiologic factor in iododerma, *529
Bechet, P. E.—Continued
Lichen planus of face, 738
Lymphangioma circumscriptum, 797
Parapsoriasis? 800
Periphlebitis nodularis necroticans, 753
Poikiloderma atrophicans vasculare, 462
Recklinghausen's disease, 631
Sarcoid, radiodermatitis or epithelioma, 743
Becker, S. W.: Chronic herpetiform eruption, 478
Mycosis fungoides, 774
Pityriasis rubra pilaris, 473
Pseudo-atrophoderma colli; hitherto undescribed condition, *53
Rheumatic nodules, 166
Ulcers (Streptococcus haemolyticus) 124
Xanthoma tuberosum multiplex and areolar xanthoma with atrophy, 469
Beerman, H.: Factors involved in leather dermatitis, *671
Rosacea complex and demodex folliculorum, *874
Beeson, B. B.: Darier's disease, 481
Epithelioma (multiple), 474
Joseph Rollet, M.D., *598
Lupus erythematosus of face with unusual lesions on back resembling superficial epithelioma, 162
Pemphigus erythematodes, 772
Pemphigus foliaceus, 127
Raynaud's disease, 165
Benjamin, H.: Leukoplakic vulvitis; lichen planus atrophicus (on abdomen and chest?); mycosis fungoides, 943
Berkovsky, M.: Pellagra, 635
Pseudopellagra (alcoholic), 635

BIOGRAPHY:

Joseph Rollet, *598

Birkman, F. W.: Recalcitrant pustular eruptions of palms and soles, *548
Bismuth: See also under Syphilis
Iodobismitol; clinical excretion of bismuth, *298
penetration of nervous system, report of clinical and laboratory study, *351
Blastomycetin: See under Blastomycosis
Blastomycosis, observations on fungi isolated from cases of blastomycosis cutis and blastomycosis pulmonalis in North America and Europe, remarks on blastomycetin, 722
Blepharitis: See Eyelids
Blood cholesterol in pellagra, 311
comparative studies of sugar content of capillaries in pathologic and in normal skin, 117
experimental study of sensitivity of skin to ultraviolet irradiation in white rats with vitamin B deficiency, 434
fats and lipoids; experimental reproduction of lipemia, 429
hemorrhage and impairment after arsphenamine, 314
lipid partition and albumin-globulin ratio in syphilis, *707
lipids in xanthoma, *228
phytopharmacologic test in dermatology; further studies and some critical estimations, *206
serum albumin in its relations to dermatology; influence of arsphenamine on serum albumin in syphilis in man and in experimental rabbits, 434
serum albumin in its relations to dermatology; serum proteins in cases of burns, 434
serum from patients with "phytid" eruptions, inhibition of fungi in cultures by, *537
serum proteins and lipoids in eczema of infants and children, 309
transferable and inhibiting substances in blood of allergic patients, 433
Bloom, D.: Carcinoma, 932
Destructive osteitis and facial paralysis in secondary syphilis, 940
Pustular psoriasis, 757

Boeck's Sarcoid: See Sarcoid
Bonar, L.: Epidermomycosis at University of California, *521

Book Reviews:
Dermatergoses or Occupational Affections of Skin; R. Prosser White, 970
Fisiologia Normale e Patologica della Cute Umana; M. Comel, 971
Handbuch der Haut- und Geschlechtskrankheiten. Volume 2; J. Jadassohn, 971
Handbuch der Haut- und Geschlechtskrankheiten; J. Jadassohn. Volume 23. Die Haut- und Geschlechtskrankheiten im Staats-, Straf-, Zivil- und Sozialrecht. Entwurf einer Geschichte der ansteckenden Geschlechtskrankheiten; J. Heller and G. Sticker, 329
Practical Treatise on Diseases of Skin; O. S. Ormsby and C. W. Finnerud, 971
Tuberculose cutanée et Tuberculides; J. Nicolas and J. Gaté, 970

Books Received, 105, 481, 603, 801
Bowen's Disease: See Cancer
Brain, spirochaetal findings in paretics treated with malaria, 308
Breast, Paget's disease of nipple, 791
Paget's diseases of nipple or eczema, 744
Bromoderma, 326
Brown, H.: Question of bismuth penetration of nervous system; report of clinical and laboratory study, *351
Brunsting, L. A.: Erythrodermia (bullous, ichthyosiform, congenital); ichthyosis plus epidermolysis bullosa, 468
Burns, powder burns, 323
removal of gunpowder by trephining, 447
serum proteins in, 434
Busman, G. J.: Hair matrix (basal cell) carcinoma, 788
Butterworth, T.: Macular atrophy of skin (anetodermia of Schweninger and Buzzi), 133
Multiple benign tumor-like new growths of skin; report of case, *893

Calcium metabolism and keloids, 114
Campbell, H. S.: Lichen planus obtusus, 921
Cancer: See also Adenoma; Sarcoma; Tumor; etc.
Cancer, 932
basal cell, 322
Bowen's precancerous dermatosis, 637, 934
chronic ulceration of soles (Bowen's disease); multiple benign superficial epitheliomas; arsenical keratoses (palms, soles, trunk), 613
conservative surgical measures facilitating radium implantation, 721
hair matrix (basal cell) carcinoma, 788
injury as causative factor in development of malignant tumors, 429
of skin in childhood, 428
rodent ulcer occurring in man and wife, 308
squamous-cell carcinoma of skin, 604
Cannon, A. B.: Darier's disease, 455
Intradermal tests in relation to arsphenamine dermatitis; study based on 256 clinical cases, *485
Late secondary syphiloderm resistant to therapy (with finding of spirochetes after extensive treatment), 451
Tuberculosis of skin, 755
Canright, C. M.: Xeroderma pigmentosum; report of case, *668
Capillaries, human, in health and disease, 430
Capillaroscopy, studies with capillary microscope, 723
studies with capillary microscope, stereoscopic examination of capillaries of skin, 723
Caro, M. R.: Cardlike scleroderma, 124
Lichen planus, 477
Caro, M. R.—Continued
Lichen planus with fatty infiltration, 130
Necrobiosis lipoidica diabeticorum (Urbach), 167
Periadenitis mucosa necrotica recurrens, 466
Carrion's Disease: See Oroya Fever
Celery itch: dermatitis due to celery in vegetable canning, 908
Cerebrospinal Fluid, is protective mechanism developed by nervous system during secondary stage of syphilis? Early treatment of syphilis and findings in spinal fluid, 912
Kahn reaction with spinal fluids containing varying amounts of syphilitic blood, *653
Chambers, S.: Charcot's joint (3 cases), 925
Leprosy, 922
Papulonecrotic tuberculid, 615
Probable syphilitic erythema nodosum, 926
Purpura annularis telangiectoides, 735
Chancre, genital, with multiple extragenital chancres, 744
of conjunctiva of upper eyelid, 609
Chancroid, lymphogranuloma inguinale and gonorrhea, 749
with positive Reenstierna test, 961
Charcot's Joints: See Tabes Dorsalis
Chargin, L.: Mercuric pigmentation, 462
Sycosis vulgaris; new method of treatment, 456, 457
Cheek, myxoma of, 739
Cheilitis: See Lips, disease
Chickenpox, agglutination in vaircella, 608
superficial abdominal gangrene as complication of varicella, 906
Cholesteremia: See Blood, cholesterol
Cholesterol, influence of cholesterol and lecithin on tendency to inflammation of skin, 723
Chorioretinitis: See Retinochoroiditis
Cilia: See Eyelashes
Clavicle, syphilis of clavicle, 905
Cobane, J. H.: Case for diagnosis, 622
Dermatitis herpetiformis, 620
Juxta-articular nodules of Lutz-Jeanselme, 445
Necrotic ulcers of unknown etiology, 620
Three cases of granuloma inguinale treated with fuadin, 619
Coccidiosis, 731
Colds: See Respiratory Tract, diseases
Combes, F. C.: Herpes menstrualis, 791
Intra-epidermal epithelioma, basal cell type (Jadassohn)?, 799
Sarcoid, 954
Comedones, nevus unilateralis comedonicus (nevus follicularis keratosis), 461
Conjunctiva, recurrent edema of lids and conjunctiva associated with dental infection, 905
Connor, W. H.: Case for diagnosis, 745
Keratodermia blennorrhagicum, 963
Lymphogranuloma inguinale, 748, 963
Lymphogranuloma inguinale; anorectal syndrome, 748
Lymphogranuloma inguinale, anorectal syndrome, esthiomene, 964
Lymphogranuloma inguinale, anorectal syndrome, tertiary syphilis, 964
Lymphogranuloma inguinale, chancroid and gonorrhea, 749
Secondary syphilis, bilateral Bell's palsy, 746
Cornbleet, T.: Argyria, 775
Avitaminosis or scurvy, 166
Dermatitis factitia, 773
Disorders of feet as cause of resistant eczematoid ringworm; their influence on amount of sweating of feet, *887
Scleroderma (unusual distribution), 132
Cornea, bilateral necrosis of cornea following use of hair dye on eyebrows and lashes, 907
Inflammation. See Keratitis
ulceration following use of Lash-Lure, 906

Cornell, V. A.: Lymphoblastoma (Hodgkin's disease) of scalp; report of case, *569
Pellagra, 635
Pseudopellagra (alcoholic), 635
Corson, E. F.: Hyperpigmentation following chemical dermatitis, 133
Parapsoriasis or syphilis, 134
Senear-Usher syndrome, 445
Cosmetics, vanishing cream, *597
Cowpox, 2 cases of milker's nodules, 117
Crawford, S.: Benign erythematoid basal cell epithelioma, 782
Branchial fistula (first ectodermal fold), 786
Case for diagnosis, 785
Herpes zoster generalisata, 789
Juvenile acrodynia, 783
Ocular pemphigus, 783
Phalangeal osteomyelitis (syphilitic) with pathologic fracture, 784
Schamberg's progressive pigmentary dermatosis, 786
Cross, F. E.: Bromoderma, 326
Erythema induratum, 145
Cummer, C. L.: Adenoma sebaceum, 139
Dermatosis papulosa nigra (Castellani), 138
Cummins, L. J.: Traumatic ulcer (right leg): late syphilis; tinea versicolor, 324
Cutis Verticis Gyrata: See under Scalp
Cylindroma of scalp, 941
Cysts, epidermal cysts following injection of viosterol, 314
sebocystomatosis or steatomatosis, 461
syphilitic synovial cyst, 730
traumatic epithelial cysts of skin, 907

Darier's Disease: See Keratosis follicularis
Davenport, K. M.: Photography in dermatology; new method, *92
Deafness, tertiary syphilis; bilateral total eighth nerve deafness, 316
Dementia Paralytica: See Paralysis, general
Demodex folliculorum and rosacea complex, *874
Depigmentation: See Pigmentation
Dermatitis: See also Acrodermatitis
actinic dermatitis with lesions resembling hydroa aestivale on face and prurigo aestivale on arms, 926
action of large doses of extract of hog's spleen in certain dermatoses, 610
Atrophicans: See Atrophy
celery itch; dermatitis due to celery in vegetable canning, 908
exfoliativa, 796
factitia?, 773
factitia, epithelioma, or dermatitis nodularis necrotica, 150
Herpetiformis: See Dermatitis multiformis
influence of cholesterol and lecithin on tendency to inflammation of skin, 723
Medicamentosa: See Arsenic; Arsphenamine; Atrophine; Bismuth; Ergosterol; Phenolphthalein; etc.
multiformis; 620, 625
multiformis, and pemphigus, etiology of, 729
multiformis, case for diagnosis (chronic herpetiform eruption), 478
multiformis; with recurrent vesicopustular lesions on palms and soles, 128
nodularis necrotica, epithelioma, or dermatitis factitia, 150
papulosa nigra, 146, 753
papulosa nigra (Castellani), 138
rattlesnake anaphylaxis associated with a generalized dermatitis, *658
recalcitrant pustular eruptions of palms and soles, *548
vegetans, report of extensive case, *282
venenata; chlorosulphonic acid cauterization as industrial accident, 115
venenata due to shoe leather, *671
venenata, due to tincture of green soap, *104
venenata due to woods, 906
venenata; hyperpigmentation following chemical dermatitis, 133
Dermatocholasis: See Skin, abnormalities
Dermatologic societies, directory of, 170, 330, 482, 642, 802, 972
Dermatophytes: See under Fungi; Trichophytosis
Dermatophytosis: See Mycosis, cutaneous
Dermatosis: See Dermatitis; Eczema; etc.
De Wolf, H. F.: Case for diagnosis, 137
Late secondary syphilis; iritis and paralysis of right fifth, seventh, eighth, eleventh and twelfth cranial nerves, 316
Lupus vulgaris with carcinomatous degeneration, 318
Lymphogranuloma inguinale, 138
Secondary syphilis; acute syphilitic meningitis, 317
Tertiary syphilis; bilateral total eighth nerve deafness, 316
Tuberculous ulcer of tongue (syphilis), 136
Xeroderma pigmentosum, 139
Diabetes, necrobiosis lipoidica diabeticorum (Urbach), 167, 931
Diathermy: See under names of various diseases
Dichlordiethylsulphide cauterization of skin, 724
Directory of dermatologic societies, 170, 330, 482, 642, 802, 972
Douche, use of filiform douche in dermatology and advantages of new apparatus, 116
Downing, J. G.: Sporotrichosis, 951
Drug Eruptions: See under names of drugs as, Arsenic; Arsphenamine; Phenolphthalein; etc.
Duemling, W. W.: Dystrophy of hair and nails; keratoderma of palms and soles; hypothyroidism, 163
Xanthoma palpebrarum and tuberosum multiplex, 123
Duhring's Disease: See Dermatitis multiformis
Durand-Nicolas-Favre's Disease: See Lymphogranuloma inguinale
Dyschromatosis universalis hereditaria, previously undescribed anomaly of pigmentation, 433
Dyshidrosis: See under Sweat and Sweat Glands
Dyskeratosis: See Keratosis

Ear, epithelioma of; difficulties in its treatment with radiation, *270
Ebert, M. H.: Cutis verticis gyrata, 129
Darier's disease, 481
Epithelioma (multiple), 474
Kaposi's sarcoma, 480
Lupus erythematosus of face with unusual lesions on back resembling superficial epithelioma, 162
Multiple epithelial nevi, 765
Pemphigus erythematodes, 772
Pemphigus foliaceus, 127
Pityriasis rubra of Hebra, 473
Raynaud's disease, 165
Tuberculosis cutis; multiple sarcoids, 145
Eczema, Bakers': See Bakers' itch
contact eczema due to clothing, 906
eczematous changes and gastric function, 433
infection with Ducrey bacillus with eczematous eruption, 954
mechanism of urticarial idiosyncrasy to egg white in eczematous child, 912
or Paget's disease of nipple, 744
serum proteins and lipoids in eczema of infants and children, 309
Edema, generalized, consecutive to intravenous injection of sodium thiosulphate, 610
recurrent, in glabellar region, 737
recurrent, of eyelids and conjunctiva associated with dental infection, 905
Egg, mechanism of urticarial idiosyncrasy to egg white in eczematous child, 912
Elephantiasis of lower lip, 917
of scrotum, 738
vulvar, syphilitic origin of, 606

Eller, J. J.: Case for diagnosis, 736
Recurrent edema in glabellar region, 737
Rosacea-like tuberculid of Lewandowsky, 630
Endocrine Glands, acanthosis nigricans: case of benign form in adult investigated from aspect of endocrine dysfunction, *691
Engman, M. F.: Lipids of skin surface, *12
Ephedrine dermatoses; clinical and experimental study of personal case with review of literature, 907
Epidermolysis bullosa dystrophica combined with keratosis palmaris et plantaris striata, 119
bullosa dystrophica, sodium chloride metabolism in, 315
bullosa hereditaria dystrophica, 725
bullosa in brothers, 929
bullosa, poikiloderma-like condition of soles (sequelae of epidermolysis bullosa), 325
Epidermomycosis: See Mycosis, cutaneous
Epidermophytosis: See Mycosis
Epithelioma adenoides cysticum, Brooke, 435
and cutaneous horn, 914
and trauma, 310
benign erythematoid basal cell epithelioma, 782
calcifying, of skin, 725
chronic ulceration of soles (Bowen's disease); multiple benign superficial epitheliomas; arsenical keratoses (palms, soles, trunk), 613
dermatitis factitia or dermatitis nodularis necrotica, 150
intra-epidermal epithelioma, basal cell type (Jadassohn)?, 799
lupus erythematosus of face with unusual lesions on back resembling superficial epithelioma, 162
multiple, 474
multiple, and pigmentary dermatosis in Negro boy, *408
multiple benign epithelioma of scalp (so-called turban tumor, endothelioma capitis, cylindroma of scalp or Spiegler's tumor), 941
of ear; difficulties in treatment with radiation, *270
of lids, treatment by radium, 610
of lip with reference to lymph node metastases, 722
pigmented basal cell epithelioma, 773
sarcoid or radiodermatitis, 743
squamous cell epithelioma of chin, 959
Epstein, N. N.: Keratosis follicularis, 438
Ergosterol, irradiated; epidermal cysts following injection of viosterol, 314
Erysipelas and mycosis fungoides, 907
Erythema, case for diagnosis, 465
erythème annulaire centrifuge (Darier), 625
induratum, 145, 750
induratum or erythema nodosum?, 793
multiforme, 161
multiforme, atrophoderma and keloidal scars following, 798
multiforme bullosum, 454
nodosum and later tuberculosis, 729
nodosum, experimental proof of tuberculous nature, 311
nodosum, family epidemic, 725
nodosum, incubation time, 312
nodosum or erythema induratum?, 793
nodosum, probable syphilitic, 926
tertiary circinate erythema with sclerosis redux, 115
ulerythema ophryogenes, 934
Erythrodermia (bullous, ichthyosiform, congenital) or ichthyosis plus epidermolysis bullosa, 468
malignant; aleukemic leukemia, 766
pityriasis rubra pilaris generalisata resembling figured erythrodermia, 724
Erythroplasia of Queyrat, 633
Esthiomene; lymphogranuloma inguinale, anorectal syndrome, esthiomene, 964
Exanthems due to gonococcus, 435
Excoriations, neurotic, 445
Eye, syphilis, rare cases of, 311
Eyelashes, bilateral necrosis of cornea following use of hair dye on eyebrows and lashes, 907
Eyelid, chancre of conjunctiva of upper eyelid, 609
chronic blepharitis of many years' duration in case of sycosis vulgaris treated by azochloramide in poppy-seed oil, 763
epitheliomas treated by radium, 610
recurrent edema of lids and conjunctiva associated with dental infection, 905

Face, annular syringocystadenoma of forehead, 609
basal cell carcinoma, 322
recurrent edema in glabellar region, 737
tuberculodermas, *251
Feet: See Foot
Felt, H.: Miliary disseminated lupoid (sarcoid), 751
Ulerythema ophryogenes, 934
Feldman, S.: Manifestations on mucous membranes in case of lymphatic leukemia, 966
Xanthoma tuberosum multiplex, 967
Felsol, ioderma from asthma remedy, 905
Fetus, elastic tissue in fetal skin, *57
Fever Therapy: See Malaria therapy; Typhoid vaccine
Fibroma, identity of adenoma sebaceum, neurofibromatosis and subungual fibromatosis, 116
Fingers, clubbed fingers with onychogryposis, 730
phalangeal osteomyelitis (syphilitic) with pathologic fracture, 784
Finnerud, C. W.: Adenoma sebaceum (familial), 472
Epithelioma, dermatitis factitia or dermatitis nodularis necrotica, 150
Erythroderma (malignant); aleukemic leukemia, 766
Fisher, J. E.: Case for diagnosis, 962
Sarcoid, 780
Fistula, branchial (first ectodermal fold), 786
Flatfoot: See Foot, flat
Foerster, H. R.: Cutis verticis gyrata, with associated pituitary disease, 164
Sarcoid, 160
Foerster, O. H.: Cutis verticis gyrata, with associated pituitary disease, 164
Sarcoid, 160
Folliculitis decalvans et atrophicans (Little), 752
decalvans or pseudopelade with unusual manifestations, 461
Foot, disorders of feet as cause of resistant eczematoid ringworm; their influence on amount of sweating of feet, *887
flat, and epidermomycosis, *356
poikiloderma-like condition of soles (sequelae of epidermolysis bullosa), 325
pustular eruptions of palms and soles, recalcitrant, *548, 741
Forehead: See Face
Fordyce Disease: See Fox-Fordyce disease
Fox, H.: Cutaneous horn developing on possible melanoma, 792
Cutaneous leprosy of long incubation period, treated by intracutaneous injections of chaulmoogra oil, 120
Dermatitis herpetiformis, 625
Dermatophytosis of penis?, 795
Erythema induratum or erythema nodosum, 793
Herpes zoster and herpes simplex recurrens, 800
Lupus erythematosus, 121
Melanoma; result of treatment at end of 4 years, 953
Report on case previously presented, 123

Fox-Fordyce disease, 313, 446
Frambesia, substitute for Wassermann test for up-country work, with observations on 3-amino-4-hydroxyphenyl dichlorarsine hydrochloride in yaws, 310
  symptomatology of yaws in Liberia; goundou and gangosa, 608
Fraser, J. F.: Paget's disease of nipple, 791
  Paget's disease of nipple or eczema, 744
Friedman, R.: Acute lupus erythematosus, 617
Frost, K.: Syphilitic synovial cyst, 730
Frostbite, capillary microscope studies, 118
Fuadin in granuloma inguinale, 619
Fuchs, A. W.: Photography in dermatology; new method, *92
Fungi: See also Actinomycosis; Blastomycosis; Moniliasis; Mycosis; Ringworm; etc.
  inhibition in cultures by blood serum from patients with "phytid" eruptions, *537
  schizosaccharomyces hominis Benedek, 116
  use of phenylmercuric nitrate in tinea and yeast infections of skin, 906
Furunculosis, treatment of furunculosis and multiple abscesses in nursling by immunohemotherapy, 312

Gammel, J. A.: Actinomycosis without granules, *287
Ganglioneuroma, 162
  multiple, of skin; report of case with differential diagnosis from reticulo-histiocytic granuloma, neuroma, xanthoma and Recklinghausen's disease of skin, *26
Gangosa, symptomatology of yaws in Liberia; goundou and gangosa, 608
Gangrene, superficial abdominal gangrene as complication of varicella, 906
Garfield, W. T.: Lichen planus and syphilis, 944
Garner, V. C.: Pellagra secondary to alcoholism, 444
Gilman, R. L.: Lichen planus hypertrophicus, 446
Gilmour, A. J.: Lupus erythematosus disseminatus, 916
  Radiodermatitis, 121
Gingivitis: See Gums, inflammation
Glaze, A. L.: Vanishing cream, *597
Godefroy French Hair Coloring (Larieuse), bilateral necrosis of cornea following use of hair dye on eyebrows and lashes, 907
Goldman, L.: Cutaneous reactions with "purified" oidiomycin, *564
Goldmann, B. A.: Case for diagnosis, 787
Goldstein's Disease: See Telangiectasis
Gonococci, exanthems due to, 435
Gonorrhea, lymphogranuloma inguinale and chancroid, 749
Goodman, H.: Results of intradermal tests with various vaccines using measured amounts of nitrogen, 935
Goundou, symptomatology of yaws in Liberia; goundou and gangosa, 608
Grace, A. W.: Acanthosis nigricans; case of benign form in adult investigated from aspect of endocrine dysfunction, *691
  Pemphigus; effect of pemphigus serum on leukocytic picture of rabbits, *885
Granuloma annulare, 613, 637
  annulare, etiology with reference to tuberculous theory, *189
  annulare of hands and feet; tuberculids of body, 940
  inguinale and abortive Recklinghausen's disease, 446
  inguinale, 3 cases treated with fuadin, 619
  multiple ganglioneuromas of skin; report of case with differential diagnosis from reticulohistiocytic granuloma, neuroma, xanthoma and Recklinghausen's disease of skin, *26
Granuloma—Continued
  progressive lethal granulomatous ulceration of nose, 607
  tuberculous, 453
Greenbaum, S. S.: Abortive Recklinghausen's disease and granuloma inguinale, 446
  Case for diagnosis, 622
  Dermatitis herpetiformis, 620
  Juxta-articular nodules of Lutz-Jeanselme, 445
  Necrotic ulcers of unknown etiology, 620
  Removal of gunpowder by trephining, 447
  Three cases of granuloma inguinale treated with fuadin, 619
Greene, C. E.: Pityriasis rubra pilaris, 323
Greenhouse, C. A.: Ichthyosis hystrix with radium sequelae, 640
  Lymphoblastoma (Hodgkin's disease) of scalp; report of case, *569
Greenwood, A. M.: Monilial infection of skin; report of fatal case, *574
Griggs, L. H.: Acetarsone in neurosyphilis, *645

Gross, P.: Anetodermia maculosa, 327
  Erythema multiforme bullosum, 454
  Folliculitis decalvans et atropicans (Little), 752
  Hyperkeratosis of palms and soles and backs of hands, 752
  Parapsoriasis lichenoides chronica with varioliform lesions, 449
  Poikiloderma-like condition of soles (sequelae of epidermolysis bullosa), 325
  Pseudopelade with unusual manifestations or folliculitis decalvans, 461
  Pyodermia chronica papillaris et exulcerans, 328
  Rhinoscleroma, 452
  Urticaria pigmentosa (solitary lesion), 451, 764
Gums, inflammation; streptococcic hypertrophic gingivitis, *422
Gunpowder removed by trephining, 447
Guy, W. H.: Acquired telangiectasia, 778
  Closing remark, 789
  Cryptococcic infection of palate, 781
  Familial telangiectasia, 778
  Mycosis fungoides, 783
  Scleredema, 777
  Scleroderma, 779

Haberman's Disease: See Pityriasis lichenoides varioliformis et acuta
Hair dye, bilateral necrosis of cornea following use of hair dye on eyebrows and lashes, 907
  dystrophy of hair and nails; keratoderma of palms and soles; hypothyroidism, 163
Hand, pustular eruptions of palms and soles, *548, 741
Hansen's Disease: See Leprosy
Hanzlik, P. J.: Iodobismitol; clinical excretion of bismuth, *298
Hasselmann, C. M.: Lupus erythematosus (discoideus) in tropics; first report of cases from Philippine Islands and investigation on occurrence of Langhans' giant cells, *585
Hecht, J. J.: Sarcoid, 780
Hedge, H. M.: Lichen scrofulosorum, 776
Heliotherapy, excessive solar and phototherapeutic irradiation; causative factor in certain diseases of skin, *221
Hemangioma cavernosum congenitum, fatal case of, 315
  spastic paraplegia resulting from hemangioma of back extending to spine in person with syphilis, 636
Herpes gestationis, 443
  iris of unusual duration, 622
  menstrualis, 791
  simplex recurrens and herpes zoster, 800
  zoster and herpes simplex recurrens, 800
  zoster generalisata, 789

Herrick, R.: Practical clinical and laboratory aspects of precipitation tests for syphilis, *835
Hodgkin's Disease: See Lymphogranuloma
Hollander, L.: Lichen planus, 786
Melanoma of temple with metastases to glands, 788
Myeloid leukemia with cutaneous manifestations, *821
Sarcoid, 780
Sarcoid of Boeck, *387
Vascular nevus, 779
Xanthoma tuberosum multiplex, 786
Hopkins, J. G.: Darier's disease, 455
Urticaria; etiologic observations, *358
Hopkins, R.: Multiple epitheliomas and pigmentary dermatosis in Negro boy, *408
Horn, cutaneous horn and epithelioma, 914
cutaneous, developing on possible melanoma, 792
Hyde, G. W.: Lupus erythematosus disseminatus, 930
Hydroa aestivale, 443
aestivale, acquired adult type, 768
aestivale; actinic dermatitis with lesions resembling hydroa aestivale on face and prurigo aestivale on arms, 926
Hyperhidrosis: See under Sweat and Sweat Glands
Hyperkeratosis: See Keratosis
Hypodermolithiasis, 909
Hypothyroidism: See Thyroid, hypothyroidism

Ichthyosis hystrix with radium sequelae, 640
or parapsoriasis, 156
plus epidermolysis bullosa or erythrodermia (bullous, ichthyosiform, congenital), 468
Immunity, persistence after abolition of allergy by desensitization, 431
relation between acid or alkaline diet and immunity, 431
Industrial disease; chlorosulphonic acid cauterization as industrial accident, 115
Influenza and grip, eruptions in, 729
Injections, intravenous, tourniquet for, *717
Iododerma from asthma remedy (Felsol), 905
iodized table salt as etiologic factor in iododerma, *529
Iodobismitol: See Bismuth
Iritis, late secondary syphilis, iritis and paralysis of right fifth, seventh, eighth, eleventh and twelfth cranial nerves, 316

Jacob, F. M.: Acquired telangiectasia, 778
Cryptococcic infection of palate, 781
Sarcoid, 780
Scleroderma, 779
Jacobson, H. P.: Coccidiosis, 731
Lupus vulgaris with tuberculous adenitis, 928
Jacoby, R.: Scleroderma, 947
Jamieson, R. C.: Lupus erythematosus disseminatus, 930
Johnson, D. W.: Dermatitis due to tincture of green soap, *104
Josephson, E. M.: Leukonychia and "colds" secondary to disturbances of metabolism, *703

Kahn Test: See under Syphilis
Kala-Azar: See Leishmaniasis
Kaposi's Disease: See Xeroderma pigmentosum
Karelitz, M. B.: Intradermal tests in relation to arsphenamine dermatitis; study based on 256 clinical cases, *485
Kastlin, G. J.: Myeloid leukemia with cutaneous manifestations, *821
Kelly, R. J.: Recalcitrant pustular eruptions of palms and soles, *548
Keloid, 933
and calcium metabolism, 114
Keloid—Continued
atrophoderma and keloidal scars following erythema multiforme, 798
Keratitis, interstitial, with scars of tertiary syphilis, 444
Keratodermia blennorrhagicum, 963
Keratosis: See also Ichthyosis
blennorrhagica, psoriasis or dermatophytosis, 319
chronic ulceration of soles (Bowen's disease); multiple benign superficial epitheliomas; arsenical keratoses (palms, soles, trunk), 613
dystrophy of hair and nails; keratoderma of palms and soles; hypothyroidism, 163
follicularis; Darier's disease, 147, 438, 455, 481, 610, 612
hyperkeratosis of palms and soles and backs of hands, 752
of lower lip, 961
palmaris et plantaris, 935
palmaris et plantaris striata combined with epidermolysis bullosa dystrophica, 119
porokeratosis (Mibelli), report of its occurrence in Negro, *20
Kesten, B. M.: Urticaria; etiologic observations, *358
Kice, L.: Lupus vulgaris, 790
Klauder, J. V.: Interstitial keratitis with scars of tertiary syphilis, 444
Neurotic excoriations, 445
Question of bismuth penetration of nervous system; report of clinical and laboratory study, *351
Klien, B.: Pseudoxanthoma elasticum; angioid streaks of retina; old chorioretinitis, 147
Koilonychia: See Nails, diseases
Kooyman, D. J.: Lipids of skin; influence of some factors on albino rat, *342
Lipids of skin surface, *12
Krasnow, F.: Lipid partition and albumin-globulin ratio in syphilis, *707

Lane, J. E.: Francois-Xavier Swediaur, *80
La Rocco, C. G.: Adenoma sebaceum, 139
Dermatosis papulosa nigra (Castellani), 138
Lashinsky, I.: Acrodermatitis chronica atrophicans with healed ulcerations, 968
Idiopathic hemorrhagic sarcoma, 144
Lash-Lure, corneal ulceration following use, 906
Lawless, T. K.: Leukemia, chronic, monocytic and myelogenous (Naegeli type), 155
Oriental sore, 155
Tularemia, 159
Leather, factors involved in leather dermatitis, *671
Lecithin, influence of cholesterol and lecithin on tendency to inflammation of skin, 723
Legge, R.: Epidermomycosis at University of California, *521
Lehmann, C. F.: Epithelioma of ear; difficulties in treatment with radiation, *270
Leishmaniasis, diagnostic value of serum protein changes in kala-azar, 607
mucocutaneous leishmaniasis of nasal cavity, 910
oriental sore, 155
Leprosy, 922
comparative complement-fixation tests in leprosy, tuberculosis and syphilis, 432
cutaneous, of long incubation period treated by chaulmoogra oil, 120
Lerner, C.: Leukonychia and "cold," secondary to disturbances of metabolism, *703
Leukemia, aleukemic, and erythroderma (malignant) 766
chronic, monocytic and myelogenous (Naegeli type), 155
familial occurrence, 436
lymphatic, 135

Leukemia—Continued
manifestations on mucous membranes in case of lymphatic leukemia, 966
myeloid, with cutaneous manifestations, *821
Leukoderma: See Vitiligo
Leukokeratosis: See Keratosis
Leukomelanoderma: See Pigmentation
Leukonychia: See under Nails
Leukoplakia or lichen planus confined to mouth, 619
Leukosarcoma, primary, of skin, 908
Levin, E. A.: Torulosis, 747
Lewis, G. M.: Ringworm of scalp; report of 3 cases due to Microsporon lanosum with tendency to spontaneous recovery, *890
Lichen chronicus simplex, 464
nitidus, 910
planus, 477, 786
planus and parapsoriasis, 131
planus and syphilis, 944
planus atrophicus on abdomen and chest, leukoplakic vulvitis and mycosis fungoides, 943
planus, generalized, 735
planus, generalized and hypertrophic, 932
planus hypertrophicus, case for diagnosis, 446
planus-like eruption and melanosis following antisyphilitic therapy, 469
planus, linear, or nevus unilateralis, 454
planus obtusus, 921
planus of face, 738
planus of mouth, 795
planus or leukoplakia confined to mouth, 619
planus or pityriasis rosea, 914
planus with alopecia areata in child, 131
planus with fatty infiltration, 130
ruber planus vulvae case resistant to arsenic but cured by acetarsone, 118
scrofulosorum, 776
scrofulosus; tuberculosis of hypoderm (Wende), 134
spinulosus, 733
spinulosus; tinea capitis with associated generalized lichen spinulosus (microsporid), 127
urticatus: See Urticaria papulosa
Lieberthal, D.: Epidermomycosis and flatfoot, *356
Lieberthal, E. P.: Epidermomycosis and flatfoot, *356
Light, actinic dermatitis, 926
xeroderma pigmentosum; study in sensitivity to light, *858
Lindsay, H. C. L.: Clubbed fingers with onychogryposis, 730
Syringocystadenoma?, 922
Lingua: See Tongue
Lipemia: See Blood, fats and lipoids
Lipids of skin, *342
of skin surface, *12
Lips, disease; cheilitis exfoliativa, 796
elephantiasis of lower lip, 917
epithelioma, with reference to lymph node metastases, 722
Lounsberry, C. R.: Rattlesnake anaphylaxis associated with generalized dermatitis, *658
Loveman, A. B.: Kahn reaction with spinal fluids containing varying amounts of syphilitic blood, *653
Lowenfish: Acanthosis nigricans (juvenile benign form), 763
Ludy, J. B.: Lymphatic leukemia, 135
Lupus: See also Tuberculosis
erythematosus, 121, 734
erythematosus, acute, 617
erythematosus, acute, disseminated, thrombopenia in, *700
erythematosus before puberty, 607
erythematosus (discoideus) in tropics; first report of cases from Philippine Islands and investigations on occurrence of Langhans' giant cells, *585
Lupus—Continued
erythematosus disseminatus, 797, 916, 930
erythematosus, extensive, 764
erythematosus in child, 927
erythematosus of face with unusual lesions on back resembling superficial epithelioma, 162
erythematosus, unusual circumoral scarring and extensive involvement of scalp and oral mucous membrane, 169
perino, 732
vulgaris, 165, 790, 946
vulgaris of flat atrophic type (under dietetic regimen), 634
vulgaris or sarcoid, 448
vulgaris with carcinomatous degeneration, 318
vulgaris with tuberculous adenitis, 928
Lymph Nodes, cutaneous generalized lymphosarcomatosis secondary to primary tumor of lymphatic glands of groin, 910
immunologic studies of spirochetoses; spirochetes in lymph glands and spleen of rabbit intravenously reinfected, 727
lupus vulgaris with tuberculous adenitis, 928
treatment of cancerous or potentially cancerous cervical lymph nodes, 429
Lymphangioma circumscriptum, 797
report on case shown at April meeting, 635
Lymphoblastoma: See Lymphogranuloma
Lymphogranuloma: See also Granuloma
experimental studies on lymphomatosis of mice, 604
genital-ano-rectal lymphogranulomatosis of male, 722
Hodgkin's disease of scalp, report of case, *569
inguinale, 138, 143, 152, 153, 439, 748, 963
inguinale, anorectal syndrome, 748
inguinale, anorectal syndrome and Nicolas-Favre disease, 114
inguinale, anorectal syndrome, esthiomene, 964
inguinale, anorectal syndrome, tertiary syphilis, 964
inguinale, chancroid and gonorrhea, 749
inguinale (lymphopathia venerea) treated with Frei vaccine, 958
lymphoblastoma, 760, 767
Lymphosarcoma, cutaneous generalized lymphosarcomatosis secondary to primary tumor of lymphatic glands of groin, 910
Lynch, F. W.: Elastic tissue in fetal skin, *57
Systematized amyloidosis of skin and muscles, *805
Xeroderma pigmentosum; study in sensitivity to light, *858
Lyons, M. A.: Lipid partition and albumin globulin ratio in syphilis, *707

McCarthy, F. P.: Lupus vulgaris, 946
Machacek, G. A.: Darier's disease, 455
Macht, D. I.: Phytopharmacologic test in dermatology; further studies and some critical estimations, *206
MacKee, G. M.: Spiegler-Fendt's sarcoid, 952
McKeever, W. H.: Recurrence of infection of feet due to ringworm fungus, *526
MacNeal, H. P.: Tourniquet for intravenous procedures, *717
Macroglossia: See under Tongue
Madden, J. F.: Herpes gestationis, 443
Kraurosis vulvae, 442
Pemphigus vulgaris, 441
Majocchi's Disease: See Purpura annularis telangiectodes
Malaria, cause of positive Wassermann reaction in, 433
therapy; effect of lipoid therapy on clinical course of dementia paralytica and neurosyphilis in patients not previously inoculated as well as in those previously inoculated with malaria, 726
therapy; spirochaetal findings in brain of paretics treated with malaria, 308

Maloney, E. R.: Atrophoderma and keloidal scars following erythema multiforme, 798
Lupus erythematosus disseminatus, 797
Martin, C. H.: Carcinoma, 932
Maxwell, E. S.: Acute interstitial myocarditis; report of case following severe dermatitis due to sulphur ointment, *382
Mehrtens, H. G.: Iodobismitol; clinical excretion of bismuth, *298
Meinicke flocculation reaction, substitute for Wassermann test for up-country work, with observations on 3-amino-4-hydroxyphenyl dichlorasine hydrochloride in yaws, 310
clarification reaction II in syphilis, 728
Melanin Pigmentation; Melanoderma: See Pigmentation
Melanoma, cutaneous horn developing on possible melanoma, 792
of temple with metastases to glands, 788
result of treatment at end of 4 years, 953
Melanosarcoma, 955
Melanosis: See Pigmentation
Melubrin: See Amidopyrine
Mendelsohn, H. V.: Sensitization tests; their value in dermatology, *845
Meningitis, secondary syphilis; acute syphilitic meningitis, 317
Mercurial pigmentation, 462
Metabolism, leukonychia and "cold," secondary to disturbances of metabolism, *703
Metasyphilis: See Syphilis, congenital
Michael, J. C.: Blood lipids in xanthoma, *228
Etiology of granuloma annulare with reference to tuberculous therapy, *189
Michelson, H. E.: Angiolupoid or tertiary syphilis, 439
Hydroa aestivale, 443
Systematized amyloidosis of skin and muscles, *805
Tuberculodermas of face, *251
Micrococcus, further observations on Micrococcus myceticus and Micrococcus metamyceticus, 608
Microsporon felineum, ringworm in adult due to, 609
lanosum, report of 3 cases of ringworm of scalp due to Microsporon lanosum with tendency to spontaneous recovery, *890
Milia in pemphigus, 154
Milker's Nodules: See Cowpox
Miller, H. C.: Ringworm of scalp; report of 3 cases due to Microsporon lanosum with tendency to spontaneous recovery, *890
Mitchell, J. H.: Dermatitis herpetiformis with recurrent vesicopustular lesions on palms and soles, 128
Erythema? 465
Lichen planus with alopecia areata in child, 131
Molds: See Fungus
Moles: See Nevus
Moniliasis, chronic paronychia due to Monilia, 310
monilial infection of skin, report of fatal case, *574
Montgomery, H.: Ganglioneuroma, 162
Multiple ganglioneuromas of skin; report of case with differential diagnosis from reticulohistiocytic granuloma, neuroma, xanthoma and Recklinghausen's disease of skin, *26
Morphea: See also Scleroderma
Morphea, 437
Mouth, cancer, 721
leukoplakia or lichen planus confined to mouth, 619
lichen planus, 795
Mucous Membranes, manifestations of lymphatic leukemia on, 966
Muir, K. B.: Pseudo-atrophoderma colli; hitherto undescribed condition, *53
Muscles, degeneration and regeneration; nodular myolysis of tongue, 114
systematized amyloidosis of skin and muscles, *805
Mycosis: See also Actinomycosis; Blastomycosis
cutaneous; epidermomycosis and flatfoot, *356
cutaneous; epidermomycosis at University of California, *521
dermatophytosis of penis?, 795
fungoides, 159, 440, 627, 739, 774, 783
fungoides and erysipelas, 907
fungoides, leukoplakic vulvitis and lichen planus atrophicus (on abdomen and chest), 943
fungoides (premycotic stage), 641
growth-repressing and killing effect of various chemical substances on epidermophyton rubrum, epidermophyton interdigitale and trichophyton pedia A and B, 723
inhibition of fungi in cultures by blood serum from patients with "phytid" eruptions, *537
psoriasis, dermatophytosis or keratosis blenorrhagica, 319
Myocarditis, acute interstitial myocarditis; report of case following severe dermatitis due to sulphur ointment, *382
Myolysis: See Muscles, degeneration and regeneration
Myxedema: See also Thyroid, hypothyroidism
localized, 438
Myxoma of cheek, 739

Nails: See also Paronychia
argyrosis of nail beds, 624
clubbed fingers with onychogryposis, 730
diseases, "koilonychia e stomacho," 728
dystrophy of hair and nails; keratoderma of palms and soles; hypothyroidism, 163
leukonychia and "colds" secondary to disturbances of metabolism, *703
onychia and paronychia due to fungi of yeast-like tyne, their pathogenic importance, 611
rare tumors of nail bed (neuromyo-arterial glomus tumors or arterial angioneuromyoma), 118
unusual ungual condition in 2 pork-butchers, 115
Necrobiosis lipoidica diabeticorum (Urbach), 167, 931
Nerve, auditory, involvement of eighth nerve in syphilis with reference to results of treatment, 721
optic, and pentavalent arsenicals, 909
Nervous System, alterations in thallium poisoning; lesions of peripheral nerves, particularly of perifollicular nerve endings, 113
bismuth penetration, report of clinical and laboratory study, *351
leukomelanoderma due to injury of vegetative nervous system caused by arsphenamine medication, 435
Syphilis: See Syphilis
Netherton, E. W.: Angiokeratoma or multiple angioma, 965
Case for diagnosis, 748
Neurofibromatosis, 631, 924
abortive Recklinghausen's disease and granuloma inguinale, 446
identity of adenoma sebaceum, neurofibromatosis and subungual fibromatosis, 116
multiple ganglioneuromas of skin; report of case with differential diagnosis from reticulohistiocytic granuloma, neuroma, xanthoma and Recklinghausen's disease of skin, *26
with lesion on tongue, 918
Neuroma, multiple ganglioneuromas of skin; report of case with differential diagnosis from reticulohistiocytic granuloma, neuroma, xanthoma and Recklinghausen's disease of skin, *26
Neurosyphilis: See Syphilis, neurosyphilis
Neurotic excoriations, 445

Nevocarcinoma: See Nevus
Nevus, blue: See Angioma
endotheliomatodes, 117
multiple epithelial nevi, 765
nevocarcinoma of left thigh, 463
unilateral psoriasis or nevus, 626
unilateralis comedonicus (nevus follicularis keratosis), 461
unilateralis or linear lichen planus, 454
vascular, 779
vascular, importance of early treatment, 310
vascularis papillomatosus, 120
Nicholas, H. O.: Blood lipids in xanthoma, *228
Nicholas-Favre's Disease: See Lymphogranuloma inguinale
Niles, H. D.: "Consecutive" depigmentation, *240
Nisbet, T.: Darier's disease, 612
Nodes, hypodermolithiasis, 909
juxta-articular and syphiloderm (late extensive) with atrophy, 775
juxta-articular (Jeanselme), 115
juxta-articular (Lutz-Jeanselme), 445
Milker's: See Cowpox
nodule on right cheek, 740
rheumatic nodules, 166
scleroderma with calcareous nodules, 771
Nomland, R.: Amyloidosis (localized, lichen) of skin, 470
Atrophy (macular) in congenital syphilis, 776
Dermatitis papulosa nigra, 146
Prurigo nodularis, 150
Pseudoxanthoma elasticum: angioid streaks of retina; old chorioretinitis, 147
Scleroderma with calcareous nodules, 771
Syphiloderm (late extensive) with atrophy and juxta-articular nodes, 775
Tuberculosis cutis; multiple sarcoids, 145
Northrop, P.: Streptococcic hypertrophic gingivitis, *422
Nose, progressive lethal granulomatous ulceration of nose, 607

Obermayer, M. E.: Chronic herpetiform eruption, 478
Mycosis fungoides, 774
Pityriasis rubra pilaris, 473
Rheumatic nodules, 166
Xanthoma tuberosum multiplex and areolar xanthoma with atrophy, 469

OBITUARIES:
Crutchfield, E. D., 427
Highman, Walter J., 719
Lane, J. E., 106
Schamberg, Jay Frank, 901
White, R. Prosser, 601

Occupational Diseases: See Industrial diseases
Oidiomycin, cutaneous reactions with "purified" oidiomycin, *564
O'Leary, P. A.: Erythrodermia (bullous, ichthyosiform, congenital); ichthyosis plus epidermolysis bullosa, 468
Ganglioneuroma, 162
Multiple ganglioneuromas of skin; report of case with differential diagnosis from reticulohistiocytic granuloma, neuroma, xanthoma and Recklinghausen's disease of skin, *26
Oliver, E. A.: Acrodermatitis chronica atrophicans, 126
Acromegaly in form of cutis verticis gyrata, 164
Atrophy (idiopathic) with poikiloderma-like changes, 156
Darier's disease, 147
Prurigo nodularis, 150
Oliver, E. L.: Basal cell carcinoma, 322
Majocchi's disease (purpura annularis telangiectodes), 322
Onychia: See under Nails
Onychogryphosis: See under Nails
Oriental Sore: See Leishmaniasis
Ormsby, O. S.: Atrophoderma with telangiectasia, 157
Erythema multiforme, 161
Ichthyosis or parapsoriasis, 156
Milia in pemphigus, 154
Mycosis fungoides, 159
Pemphigus atypical, 147
Pemphigus, atypical (Schmidt type), 148
Xantho-endothelioma, 770
Oroya Fever; verruca peruana or Carrion's disease, 114
Osarsol: See Syphilis, treatment
Osteitis, destructive osteitis and facial paralysis in secondary syphilis, 940
Osteomyelitis, phalangeal osteomyelitis (syphilitic) with pathologic fracture, 784
Oulmann, L.: Myxoma of cheek, 739

Pace, E. R.: Argyria 775
Dermatitis factitia, 773
Lupus vulgaris, 165
Scleroderma (unusual distribution), 132
Paget's Disease of Nipple: See under Breast
Palate, cryptococcic infection of, 781
Palsy: See Paralysis
Paralysis; bilateral Bell's palsy with secondary syphilis, 746
facial; destructive osteitis and facial paralysis in secondary syphilis, 940
general; effect of lipoid therapy on clinical course of dementia paralytica and neurosyphilis in patient not previously inoculated as well as in those previously inoculated with malaria, 726
general, spirochaetal findings in brains of paretics treated with malaria, 308
late secondary syphilis; iritis and paralysis of right fifth, seventh, eighth, eleventh and twelfth cranial nerves, 316
spastic paraplegia resulting from hemangioma of back extending to spine in person with syphilis, 636
Parapsoriasis, 800, 931
and lichen planus, 131
lichenoides chronica with several varioliform lesions, 449
or ichthyosis, 156
or syphilis, 134
Paronychia and onychia due to fungi of yeast-like type; their pathogenic importance, 611
chronic, due to monilia, 310
Parounagian, M. B.: Arsenical dermatitis (lichenoid type), 919
Arsphenamine dermatitis, 122
Atrophia cutis maculosa, 919
Elephantiasis of lower lip, 917
Elephantiasis of scrotum, 738
Genital chancre with multiple extragenital chancres, 744
Nodule on right cheek, 740
Papulonecrotic tuberculids (generalized), 122
Poikiloderma atrophicans vasculare, 915
Recklinghausen's disease with lesion on tongue, 918
Rupial syphilis, recalcitrant to treatment, 918
Peck, S. M.: Sycosis vulgaris; new method of treatment, 456, 457
Pellagra, 635
alcoholic, 441
alcoholic pseudopellagra, 635
alcoholism and, 428, 444
cholesteremia in, 311
in child 2 years old, 309
skin lesions of; experimental study, 606
Pels, I. R.: Phytopharmacologic test in dermatology; further studies and some critical estimations, *206
Pemphigus, 125
and dermatitis herpetiformis, etiology of, 729
atypical, 147
atypical (Schmidt type), 148
chronicus, value of germanin in, 117

Pemphigus—Continued
effect of pemphigus serum on leukocytic picture of rabbits, *885
erythematodes, 772
foliaceus, 127
milia in, 154
ocular, 783
phytopharmacologic test in dermatology; further studies and some critical estimations, *206
Senear-Usher syndrome, 445, 911
vegetans, 112
vulgaris, 441
vulgaris, methylthionine chloride (Macht) in, 638
vulgaris, therapeutic experiences in, 724
Penis, dermatophytosis of, 795
etiological and pathological aspects of squamous-cell carcinoma of penis among Chinese, 604
Periadenitis mucosa necrotica recurrens, 466
Periphlebitis nodularis necroticans, 753
nodularis necroticans; papulonecrotic tuberculid (aberrant unilateral eruption on leg), 632
Perlstein, M. O.: Lymphoblastoma, 767
Lymphogranuloma inguinale, 152, 153
Poikiloderma atrophicans vasculare, 158
Scurvy, 479
Tertiary syphilis, 475
Tinea capitis with associated generalized lichen spinulosus (microsporid), 127
Permar, H. H.: Myeloid leukemia with cutaneous manifestations, *821
Perspiration: See under Sweat and Sweat Glands
Phenolphthalein eruption (drug eruption), 789
Photography in dermatology, new method, *92
infra-red photographs in dermatology, 118
Phytopharmacologic test in dermatology, further studies and some critical estimations, *206
Pigmentation, "consecutive" depigmentation, *240
hyperpigmentation following chemical dermatitis, 133
leukomelanoderma due to injury of vegetative nervous system caused by arsphenamine medication, 435
lichen planus-like eruption and melanosis following antisyphilitic therapy, 469
melanoderma toxica lichenoides (Hoffmann), 113
melanosis and lichen planus-like eruption following antisyphilitic therapy, 469
melanosis of Riehl, 113
mercuric, 462
multiple epitheliomas and pigmentary dermatosis in Negro boy, *408
previously undescribed anomaly: dyschromatosis universalis hereditaria, 433
Schamberg's progressive pigmentary dermatosis, 786
Pillsbury, D. M.: Fox-Fordyce disease, 446
Tuberculosis of hypoderm (Wende); lichen scrofulosus, 134
Pink Disease: See Acrodynia
Pinta: See under Mycosis
Pituitary body, cutis verticis gyrata with associated pituitary disease, 164
Pityriasis lichenoides et varioliformis acuta, 120, 948
lichenoides et varioliformis acuta or pityriasis rosea (papulovesicular type), 450
lichenoides varioliformis et acuta (so-called Haberman's disease), 139
rosea haemorrhagica, 118
rosea-like toxicodermias clearing with pigmentation, and pityriasis rosea with pigmentation, 118
rosea or lichen planus, 914
rosea (papulovesicular type) or pityriasis lichenoides et varioliformis acuta, 450
rubra of Hebra, 473
rubra pilaris, 323, 473, 916
Pityriasis—Continued
rubra pilaris generalisata resembling figured erythrodermia, 724
versicolor in Negress, 610
Plummer, F. V.: Amyloidosis (localized, lichen) of skin, 470
Darier's disease, 147
Erythroderma (malignant); aleukemic leukemia, 766
Poikiloderma atrophicans vasculare, 158, 462, 915
atrophy (idiopathic) with poikiloderma-like changes, 156
-like condition of soles (sequelae of epidermolysis bullosa), 325
Porokeratosis: See Keratosis
Precipitin reactions, application of recent precipitation reactions for demonstration of syphilis in rabbits, 431
Prurigo aestivale; actinic dermatitis with lesions resembling hydroa aestivale on face and prurigo aestivale on arms, 926
nodularis, 150
Pruritus ani, etiology and treatment, 429
Pseudo-atrophoderma colli; hitherto undescribed condition, *53
Pseudobromoderma of Brocq, 910
Pseudopelade: See Alopecia
Pseudoxanthoma elasticum; angioid streaks of retina; old chorioretinitis, 147
Psoriasis and gold salts, 308
case for diagnosis, 957
dermatophytosis or keratosis biennorrhagica, 319
linguae, 143
pustular, 757
some aspects of psoriasis, 905
treatment by injection of scales, 908
unilateral, or nevus, 626
vulgaris, influence of pyogenic infection on, 725
Purpura annularis telangiectoides, 322, 735, 946
peculiar form of, 909
Pusey, W. A.: Acne in 1 of identical twins, *706
Pyodermia chronica papillari et exulcerans, 328
influence of pyogenic infection on psoriasis vulgaris, 725

Quinine and ultraviolet rays, 432

Radiodermatitis: See Roentgen Rays, toxicity
Radiotherapy, effects of irradiation of skin by therapeutic dose, 119
epithelioma of ear; consideration of difficulties in its treatment with radiation, *270
Radium: See under names of diseases
Rattner, H.: Acne in 1 of identical twins, *706
Pemphigus, 125
Rauschkolb, J. E.: Tuberculosis of skin; clinical report, *398
Raynaud's Disease, case for diagnosis, 165
with calcareous deposits, 930
Recklinghausen's Disease: See Neurofibromatosis
Rendu-Osler's Disease: See Telangiectasis
Respiratory Tract, diseases, leukonychia and "colds" secondary to disturbances of metabolism, *703
Retinochoroiditis pseudoxanthoma elasticum; angioid streaks of retina; old chorioretinitis, 147
Rhinoscleroma, 452
Ringworm, disorders of feet as cause of resistant eczematoid ringworm; their influence on amount of sweating of feet, *887
fungus, recurrence of infection of feet due to, *526
in adult due to Microsporon felineum, 609
of scalp; report of 3 cases due to Microsporon lanosum with tendency to spontaneous recovery, *890

Riordan, T. J.: Granuloma annulare of hands and feet; tuberculids of body, 940
Ritchie, E. B.: Practical clinical and laboratory aspects of precipitation tests for syphilis, *835
Robinson, L. B.: Sebocystomatosis or steatomatosis, 461
Robinson, S.: Syphilitic synovial cyst, 730
Rockwood, E. M.: Monilial infection of skin; report of fatal case, *574
Roentgen Rays, question of irradiation by x-rays as cause of sarcoma, 907
Therapy: See also under names of diseases
therapy; criticism of dermatologic therapy; acne vulgaris and roentgen radiation, 116
therapy; effects of irradiation by therapeutic dose, 119
toxicity; ichthyosis hystrix with radium sequelae, 640
toxicity; radiodermatitis, 121
toxicity; radiodermatitis, sarcoid or epithelioma, 743
toxicity; studies with capillary microscope, 723
Ronchese, F.: Multiple benign epithelioma of scalp (so-called turban tumor, endothelioma capitis, cylindroma of scalp or Spiegler's tumor), 941
Rosacea complex and demodex folliculorum, *874
Rosen, I.: Generalized lichen planus, 735
Lipid partition and albumin-globulin ratio in syphilis, *707
Pityriasis lichenoides and varioliformis acutis, 120
Rosenthal, T.: Bowen's disease, 637
Fixed eruption following administration of arsphenamine, 969
Leukoderma centrifugum acquisitium (Sutton), 140
Secondary macular atrophy following syphilis (atrophia maculosa syphilitica), 969
Ross, E.: Pemphigus; effect of pemphigus serum on leukocytic picture of rabbits, *885
Rostenberg, A.: Lymphogranuloma inguinale, 143
Mycosis fungoides (premycotic stage), 641
Psoriasis linguae, 143
Ulcus durum, 141
Urticaria pigmentosa aquisita in full-blooded Indian, 640
Urticaria pigmentosa in adult, 461
Rulison, R. H.: Drug eruption, 789
Rumpel-Leede phenomenon; experimentally induced passive congestion hemorrhages, 117
Ryan, M.: Powder burns, 323

Salts, iodized table salt as etiologic factor in iododerma, *529
production of tumor-like growths by inorganic salts, 611
Sarcoid, 160, 780, 954
miliary disseminated lupoid (sarcoid), 751
multiple; tuberculosis cutis, 145
of Boeck, *387
or lupus vulgaris, 448
radiodermatitis or epithelioma, 743
Spiegler-Fendt's sarcoid, 952
Sarcoma, idiopathic hemorrhagic sarcoma, 144
Kaposi's, 480, 617
question of irradiation by x-rays as cause of sarcoma, 907
Satenstein, D. L.: Cutaneous horn and epithelioma, 914
Mycosis fungoides, 739
Saunders, W. G.: Lichen chronicus simplex, 464
Papulonecrotic tuberculid, 463
Scalp, acromegaly in form of cutis verticis gyrata, 164
cutis verticis gyrata, 129
cutis verticis gyrata with associated pituitary disease, 164
lymphoblastoma (Hodgkin's disease) of scalp, report of case, *569
Scalp—Continued
multiple benign epithelioma of scalp (so-called turban tumor, endothelioma capitis, cylindroma of scalp or Spiegler's tumor), 941
Schamberg, J. F.: Acetarsone in treatment of neurosyphilis, *645
Schamberg's progressive pigmentary dermatosis, 786
Scheer, M.: Adenoma sebaceum, Balzer's type, 738
Pityriasis rosea or lichen planus, 914
Pityriasis rubra pilaris, 916
Schizosaccharomyces: See under Fungi
Schlesinger, C. R.: Sarcoid of Boeck, *387
Schmitt, C. L.: Myeloid leukemia with cutaneous manifestations, *821
Scholtz, M.: Lupus erythematosus, 734
Schorr, H. C.: Lichen planus, 477
Lichen planus and parapsoriasis, 131
Pigmented basal cell epithelioma, 773
Schwartz, H. J.: Acanthosis nigricans; benign form in adult investigated from aspect of endocrine dysfunction, *691
Chancroid (with positive Reenstierna test), 961
Melanosarcoma, 955
Psoriasis, 957
Schweninger-Buzzi type of tumor-like new growths, *219
Scleredema, 777
Sclerema: See Scleroderma
Scleroderma, 134, 779, 947
acrodermatitis chronica atrophicans with sclerodermatous changes, 731
cardilike, 124
lichenoides ("lichen albus"), 630
of left side of face and scalp (hemiatrophy), 634
of left upper extremity, 624
unusual distribution, 132
with calcareous nodules, 771
Sclerosis, adenoma sebaceum with tuberous sclerosis, 920
redux with tertiary circinate erythema, 115
Scorbutus: See Scurvy
Scrofuloderma: See Tuberculosis, Skin
Scrotum, elephantiasis of, 738
Scull, R.: Atrophy (macular) in congenital syphilis, 776
Dermatitis papulosa nigra, 146
Scurvy, case for diagnosis, 479
or avitaminosis, 166
Sebocystomatosis or steatomatosis, 461
Secretions, Internal: See Endocrine Glands
Senear, F. E.: Lupus vulgaris, 165
Lymphogranuloma inguinale, 152
Periadenitis mucosa necrotica recurrens, 466
Xanthoma tuberosum multiplex, 769
Senear-Usher Syndrome: See Pemphigus
Shaffer, L. W.: Treatment of postarsphenamine dermatitis, *173
Trichophytosis or trichophytid, 932
Silver, H.: Fixed eruption following administration of arsphenamine, 969
Pemphigus vulgaris treatment with methylthionine chloride (Macht), 638
Pityriasis lichenoides varioliformis et acuta (so-called Haberman's disease), 139
Secondary macular atrophy following syphilis (atrophia maculosa syphilitica), 969
Spastic paraplegia resulting from hemangioma of back extending to spine in person with syphilis, 636
Silver; argyria, 775
argyrosis of nail beds, 624
Skin, abnormalities, dermatochalasis (flabby skin), with attention to its pathogenesis and relationship to dermatitis atrophicans progressiva, 116
Atrophy: See Atrophy
Cancer: See Cancer
chemistry, 313

Skin—Continued
development of true mucus tissue in, 117
elastic tissue in fetal skin, *57
Lipids: See Lipids
phytopharmacologic test in dermatology, *206
studies with capillary microscope, 723
Tuberculosis: See Tuberculosis
turgor in nutritional disturbances, 314
turgor of sucklings, 314
Skolnik, E. A.: Syphiloderm (late extensive) with atrophy and juxta-articular nodes, 775
Snake Venom: See Venom
Soap, green soap, dermatitis due to tincture of, *104
Societies, dermatologic, directory of, 170, 330, 482, 642, 802, 972
Fifth Congress of Dermatologists and Syphilographers speaking French language, 307
foreign, directory of, 170, 330, 482, 642, 802, 972
International Dermatological Congress, ninth, 718
local, directory of, 171, 331, 483, 643, 803, 973
national, directory of, 170, 330, 482, 642, 802, 972
sectional, directory of, 170, 330, 482, 642, 802, 972
state, directory of, 171, 331, 483, 643, 803, 973
Society Transactions:
American Dermatological Association, 145
Bronx Dermatological Society, 139, 325, 635, 966
Central States Dermatological Society, 777
Chicago Dermatological Society, 123, 465, 765
Cleveland Dermatological Society, 136, 316, 745, 962
Detroit Dermatological Society, 463, 929
Los Angeles Dermatological Society, 612, 730, 920
Manhattan Dermatologic Society, 120, 735, 914
Minnesota Dermatological Society, 438
New England Dermatological Society, 319, 941
New York Academy of Medicine, Section of Dermatology and Syphilis, 448, 750, 932
New York Dermatological Society, 624, 789, 952
Philadelphia Dermatological Society, 133, 444, 615
San Francisco Dermatological Association, 437
Sodium chloride metabolism in epidermolysis bullosa dystrophica, 315
Thiosulphate: See Thiosulphate
Spaulding, J. B.: Iodobismitol; clinical excretion of bismuth, *298
Spine, spastic paraplegia resulting from hemangioma of back extending to spine in person with syphilis, 636
Spinner, G. J.: Case for diagnosis, 142
Granuloma annulare, 637
Spirochetoses, immunologic studies; spirochetes in lymph glands and spleen of rabbit intravenously reinfected, 727
Spleen extract, hog's, action in certain dermatoses, 610
immunologic studies of spirochetoses; spirochetes in lymph glands and spleen of rabbit intravenously reinfected, 727
syphilitic tumor associated with symptom complex of Banti, 727
Sporotrichosis, 951
Stains and Staining, cellular pathology of experimental syphilis as studied by supravital method, 606
effect of trypan blue on experimental syphilis in rabbit, 606
Staphylococci, oral immunization with virulent staphylococci and streptococci, 432
Steatocystoma multiplex, 437
Steatomatosis or sebocystomatosis, 461
Stevens, R. H.: Nevocarcinoma of left thigh, 463
Stillians, A. W.: Tularemia, 159
Stocking, L.: Kahn reaction with spinal fluids containing varying amounts of syphilitic blood, *653
Stokes, J. H.: Rosacea complex and demodex folliculorum, *874
Stomach, cancer; acanthosis nigricans; tertiary syphilis; scirrhous carcinoma of stomach (inoperable), 942
eczematous changes in skin and gastric function, 433
Stout, K. L.: Porokeratosis (Mibelli); report of its occurrence in Negro, *20
Straub, M. E.: Tourniquet for intravenous procedures, *717
Strauss, A.: Case for diagnosis, 447
Scleroderma, 134
Streptococcus haemolyticus ulcers, 124
oral immunization with virulent staphylococci and streptococcus, 432
Strickler, A.: Recurrence of infection of feet due to ringworm fungus, *526
Sugar, comparative studies of sugar content of capillaries in pathologic and in normal skin, 117
Sulphur ointment, acute interstitial myocarditis following dermatitis due to, *382
Sweat and Sweat Glands; disorders of feet as cause of resistant eczematoid ringworm; their influence on amount of sweating of feet, *887
Swediaur, Francois-Xavier Swediaur, *80
Sweitzer, S. E.: Acute alcoholic pellagra, 441
Localized myxedema, 438
Lymphogranuloma inguinale, 439
Mycosis fungoides, 440
Sycosis vulgaris, chronic blepharitis of many years' duration in case of sycosis vulgaris successfully treated by azochloramide in poppy-seed oil, 763
vulgaris, new method of treatment, 456, 457
Synovial membrane, syphilitic cysts, 730
Syphilids, follicular, 609
late secondary syphiloderm resistant to therapy (with finding of spirochetes after extensive treatment), 451
syphiloderm (late extensive) with atrophy and juxta-articular nodes, 775
Syphilis and lichen planus, 944
and tuberculosis, 912
congenital, acetarsone in, 312
congenital, acetarsone (stovarsol) by mouth in, 428
congenital; advantage of early treatment as judged by Wassermann test, 605
congenital, macular atrophy in, 776
congenital, modern conceptions, 608
congenital, solitary lesion on cheek of child with, 967
conjugal, statistical study, 721
curability of late syphilis in rabbits and question of immunity, 913
destructive osteitis and facial paralysis in secondary syphilis, 940
experimental, cellular pathology as studied by supravital method, 606
experimental, effect of trypan blue in rabbit, 606
functional changes of thyroid in florid secondary syphilis determined by Kottmann reaction, 313
Hereditary: See Syphilis, congenital
Kahn reaction with spinal fluids containing varying amounts of syphilitic blood, *653
late secondary syphilis; iritis and paralysis of right fifth, seventh, eighth, eleventh and twelfth cranial nerves, 316
late, traumatic ulcer (right leg); tinea versicolor, 324
lipid partition and the albumin-globulin ratio in, *707
Meinicke clarification reaction II in, 728
neurosyphilis, acetarsone in, *645
neurosyphilis; divided doses of typhoid vaccine in fever therapy of neurosyphilis, 906

Syphilis—Continued
neurosyphilis; effect of lipoid therapy on clinical course of dementia paralytica and neurosyphilis in patients not previously inoculated as well as those in previously inoculated with malaria, 726
neurosyphilis; involvement of eighth nerve in syphilis with reference to results of treatment, 721
neurosyphilis; is protective mechanism developed by nervous system during secondary stage of syphilis? early teratment of syphilis and findings in spinal fluid, 912
ocular, rare cases of, 311
of clavicle, 905
or parapsoriasis, 134
precipitation tests, practical clinical and laboratory aspects of, *835
rupial syphilis, recalcitrant to treatment, 918
secondary; acute syphilitic meningitis, 317
secondary; bilateral Bell's palsy, 746
secondary macular atrophy following syphilis (atrophia maculosa syphilitica), 969
serodiagnosis; application of recent precipitation reactions for demonstration of syphilis in rabbits, 431
serodiagnosis; complement-fixation tests in leprosy, tuberculosis and syphilis, 432
serodiagnosis; substitute for Wassermann test for up-country work, with observations on 3-amino-4-hydroxyphenyl dichlorarsine hydrochloride, 310
serum albumin in its relation to dermatology; influence of arsphenamine on serum albumin in syphilis in man and in experimental rabbits, 434
spastic paraplegia resulting from hemangioma of back extending to spine in person with syphilis, 636
synovial cyst due to, 730
tertiary, 475
tertiary; acanthosis nigricans; tertiary syphilis; scirrhous carcinoma of stomach (inoperable), 942
tertiary; bilateral total eighth nerve deafness, 316
tertiary interstitial keratitis with scars of, 444
tertiary, lymphogranuloma inguinale, anorectale syndrome, 964
tertiary, or angiolupoid, 439
tertiary, resistant, with negative Wassermann reaction, 959
Treatment: See also Arsphenamine; Bismuth; etc.
treatment; combined action of arsphenamine and ultraviolet rays on Spirochaeta pallida, 432
treatment, iodobismitol, clinical excretion of bismuth, *298
treatment; should patient with suspicious genital lesion receive antisyphilitic therapy in spite of the failure to demonstrate spirochetes in dark-field examination? 724
treatment with acetarsone preparation (osarsol), 726
tuberculous ulcer of tongue or syphilis, 136
Wassermann meaning and reliability of umbilical cord Wassermann tests, 605
Syphiloderm: See Syphilids
Syphilology, report on instruction regarding syphilis in American medical schools, 605
Syringocystadenoma, annular syringocystadenoma of forehead, 609
case for diagnosis, 922

Tabes dorsalis, Charcot's joint (3 cases), 925
Teeth, caries; recurrent edema of lids and conjunctiva associated with dental infection, 905

Telangiectasis, acquired, 778
familial, 778
generalized angiomatosis (telangiectasia), 907
Goldstein's disease or Rendu-Osler-Weber disease, 728
with atrophoderma, 157

Templeton, H. J.: Epidermomycosis at University of California, *521
Thrombopenia in acute disseminated lupus erythematosus, *700
Thallium acetate and thallium salicylate; experimental biologic dosage, 911
poisoning; alterations of nervous system in; lesions of peripheral nerves, particularly of perifollicular nerve endings, 113
salicylate and thallium acetate, experimental biologic dosage, 911
Thiosulphate, generalized edema consecutive to intravenous injection of sodium thiosulphate, 610
Thrombopenia in acute disseminated lupus erythematosus, *700
Throne, B.: Erythroplasia of Queyrat, 633
Thurmon, F. M.: Acanthosis nigricans; tertiary syphilis; scirrhous carcinoma of stomach (inoperable), 942
Thyroid, functional changes of thyroid in florid secondary syphilis determined by Kottmann reaction, 313
hypothyroidism; dystrophy of hair and nails; keratoderma of palms and soles; hypothyroidism, 163
Tinea barbae, recovery of Acrostalagmus cinnabarinus corda from case clinically one of tinea barbae, 723
capitis with associated generalized lichen spinulosus (microsporid), 127
use of phenylmercuric nitrate in tinea and yeast infections of skin, 906
versicolor, traumatic ulcer (right leg) or late syphilis, 324
Tobias, N.: Multiple benign tumor-like new growths of Schweninger-Buzzi type; report of case, *219
Tobin, W. W.: Acrodermatitis chronica atrophicans, 126
Scleroderma with calcareous nodules, 771
Tolmach, J. A.: Erythema induratum, 750
Nevus unilateralis comedonicus (nevus follicularis keratosis), 461
Tolman, M. M.: Purpura annularis telangiectodes (Majocchi), 946
Tongue, congenital neurofibromatous macroglossia, 431
experimentally induced epithelial proliferation of rabbit's tongue, 611
nodular myolysis of, 114
Recklinghausen's disease with lesion on tongue, 18
tuberculous ulcer of tongue or syphilis, 136
Tonnenholz, H.: Necrobiosis lipoidica diabeticorum (Urbach), 931
Torulosis, 747
Tourniquet for intravenous procedures, *717
Traub, E. F.: Case of lymphangioma shown at April meeting, 635
Cheilitis exfoliativa, 796
Dermatitis exfoliativa, 796
Keratoses of lower lip, 961
Lichen planus of mouth, 795
Lupus vulgaris, 790
Lymphoblastoma? 760
Squamous cell epithelioma of chin, 959
Unilateral psoriasis (question of nevus), 626
Trauma, injury as causative factor in development of malignant tumors, 429
Trychophytin reaction; results of intradermal tests with various vaccines using measured amounts of nitrogen; preliminary report of experimental work, 935
growth-repressing and killing effect of various chemical substances on epidermophyton rubrum, epidermophyton interdigitale and trichophyton pedis A and B, 723
Trichophytosis or trichophytid, 932
recovery of Acrostalagmus cinnabarinus Corda from case clinically one of tinea barbae, 723
universal, with formation of enormous, deep tumors, 112

Tryparsamide, fixed dermatitis due to, 606
Tubercle bacilli in blood in tuberculosis of skin, 116
Tuberculids: See under Tuberculosis, Skin
Tuberculin, tape test with tuberculin ointment, 308
Tuberculosis: See Tuberculosis, Skin; and under names of organs and regions, i.e., Tongue, tuberculosis; etc.
Tuberculosis Skin, 755
  and syphilis, 912
  clinical report, *398
  comparative complement-fixation tests in leprosy, tuberculosis and syphilis, 432
  erythema nodosum and later tuberculosis, 729
  face, *251
  histology of, 112
  of hypoderm (Wende); lichen scrofulosus, 134
  or multiple sarcoids, 145
  papulonecrotic, 463, 615
  papulonecrotic tuberculids (generalized), 122
  periphlebitis nodularis necroticans; papulonecrotic tuberculid (aberrant unilateral eruption on leg), 632
  rosacea-like tuberculid of Lewandowsky, 630
  sodium chloride in experimental tuberculosis of rabbit, 911
  tubercle bacillemia in, 116
  tuberculids of body; granuloma annulare of hands and feet, 940
Tuberosum multiplex and xanthoma palpebrarum, 123
Tularemia, 159
Tulipan, L.: Keratosis palmaris et plantaris, 935
Tumors: See also under Cancer; Sarcoma; etc.
  multiple benign tumor-like new growths of skin, report of case, *893
  multiple tumor-like nodules in skin of unknown origin, 724
  production of tumor-like growths by inorganic salts, 611
  Spiegler's, 941
  turban, 941
Twins, acne in 1 of identical twins, *706
Typhoid, divided doses of typhoid vaccine in fever therapy of neurosyphilis, 906

Ulcers, necrotic, of unknown etiology, 620
  of unknown origin, 732
  Rodent: See Cancer
  Streptococcus haemolyticus, 124
  traumatic ulcer (right leg), late syphilis or tinea versicolor, 324
  ulcus durum, 141
Ulerythema ophryogenes, 934
Ultraviolet Rays and quinine, 432
  combined action of arsphenamine and ultraviolet rays on Spirochaeta pallida, 432
  experimental study of sensitivity of skin to ultraviolet irradiation in white rats with vitamin B deficiency, 434
Umansky, M.: Solitary lesion on cheek of child with congenital syphilis, 967
Umbilical cord, meaning and reliability of umbilical cord Wassermann tests, 605
Urticaria, etiologic observations, *358
  papulosa or lichen urticatus, 310
  pigmentosa, 732
  pigmentosa aquisita in full-blooded Indian, 640
  pigmentosa in adult, 461
  pigmentosa (solitary lesion), 451, 764

Vaccines, results of intradermal tests with various vaccines using measured amounts of nitrogen, preliminary report of experimental work, 935
Valade, C. K.: Parapsoriasis, 931
van de Erve, J. M.: Practical clinical and laboratory aspects of precipitation tests for syphilis, *835
Van Dyck, L. S.: Pityriasis rosea (papulovesicular type) or pityriasis lichenoides et varioliformis acuta, 450
Vanishing cream, *597
van Rhee, G.: Raynaud's disease with calcareous deposits, 930
Van Studdiford, M. T.: Multiple epitheliomas and pigmentary dermatosis in Negro boy, *408
Varicella: See Chickenpox
Venom, rattlesnake anaphylaxis associated with a generalized dermatitis, *658
Vero, F.: Sarcoid or lupus vulgaris, 448
  Tuberculous granuloma? 453
Verruca peruana: See Oroya Fever
  sulpharsphenamine in treatment of warts, *687
Viosterol: See Ergosterol
Vitamins; avitaminosis or scurvy, 166
  A deficiency, new cutaneous manifestation in syndrome of 603
  B deficiency, experimental study of sensitivity of skin to ultraviolet irradiation in white rats with vitamin B deficiency, 434
Vitiligo, gold and sodium thiosulphate in leukoderma, 615
  leukoderma centrifugum acquisitum (Sutton), 140
  treatment with oil of bergamot in combination with ultraviolet rays, 610
Vulva, inflammation, chronic hemorrhagic vulvitis (Lipschütz), 115
  kraurosis vulvae, 442
  leukoplakic vulvitis; lichen planus atrophicus (abdomen and chest); mycosis fungoides, 943
  lichen ruber planus vulvae resistant to arsenic but cured by acetarsone, 118

Wallhauser, A.: Dermatitis vegetans; report of extensive case, *282
Wallhauser, H. J. F.: Dermatitis vegetans; report of extensive case, *282
  Naevus vascularis papilliomatosus, 120
Wander, W. G.: Epidermolysis bullosa in brothers, 929
  Lichen planus, generalized and hypertrophic, 932
Warts: See Verruca
Wassermann Reaction: See also Syphilis
  cause of positive reaction in malaria, 433
  meaning and reliability of umbilical cord Wassermann tests, 605
  substitute for up-country work with observations on 3-amino-4-hydroxyphenyl dichlorarsine hydrochloride in yaws, 310
Way, S. C.: Steatocystoma multiplex, 437
Weidman, F. D.: Herpes iris of unusual duration, 622
  Leukoplakia or lichen planus confined to mouth, 619
  Verrucous dermatosis of legs, 621
White, C. J.: Hydroa aestivale (acquired adult type), 768
Wieder, L. M.: Cutis verticis gyrata, with associated pituitary disease, 164
  Sarcoid, 160
Wien, M. S.: Lymphoblastoma, 767
  Lymphogranuloma inguinale, 152, 153
  Scurvy, 479
  Syphilis (tertiary), 475
  Tinea capitis with associated generalized lichen spinulosus (microsporid), 127
Williams, C. M.: Cutaneous manifestations of allergy, *333
  Resistant tertiary syphilis with negative Wassermann reaction, 959
Winer, L. H.: Tuberculodermas of face, *251
Wise, F.: American Board of Dermatology and Syphilology; step forward in supervision of specialism, *1

Wise, F.—Continued
Argyrosis of nail beds, 624
Erytheme annulaire centrifuge (Darier), 625
Infection with Ducrey bacillus with eczematous eruption, 954
Lupus vulgaris of flat, atrophic type, 634
Lymphogranuloma inguinale (lymphopathia venerea) treated with Frei vaccine, 958
Mycosis fungoides, 627
"Periphlebitis nodularis necroticans"; papulonecrotic tuberculid (aberrant unilateral eruption on leg), 632
Scleroderma lichenoides ("lichen albus"), 630
Scleroderma of left side of face and scalp (hemiatrophy), 634
Scleroderma of left upper extremity, 624
Wolf, C.: Idiopathic hemorrhagic sarcoma, 144
Wolf, M.: Multiple epithelial nevi, 765
Pityriasis rubra of Hebra, 473
Wood, dermatitis due to woods, 906
Woodburne, A. R.: Streptococcic hypertrophic gingivitis, *422
Wright, C. S.: Acute lupus erythematosus, 617
Kaposi's sarcoma, 617
Leukoderma treated with gold and sodium thiosulphate, 615

Xanthe-endothelioma, case for diagnosis, 770
Xanthoma, blood lipids, *228
Xanthoma—Continued
multiple ganglioneuromas of skin; report of case with differential diagnosis from reticulohistiocytic granuloma, neuroma, xanthoma and Recklinghausen's disease of skin, *26
palpebrarum and tuberosum multiplex, 123
tuberosum multiplex, 769, 786, 967
tuberosum multiplex and areolar xanthoma with atrophy, 469
Xeroderma pigmentosum, 139
pigmentosum, report of case, *668
pigmentosum; study in sensitivity to light, *858

Yaws: See Frambesia

Zakon, S. J.: Oriental sore, 155
Zeisler, E. P.: Cardlike scleroderma, 124
Lichen planus and parapsoriasis, 131
Lichen planus-like eruption and melanosis following antisyphilitic therapy, 469
Lichen planus with fatty infiltration, 130
Lupus erythematosus (unusual circumoral scarring and extensive involvement of scalp and oral mucous membrane), 169
Necrobiosis lipoidica diabeticorum (Urbach) 167
Pemphigus, 125
Zona: See Herpes Zoster
Zoster: See Herpes Zoster

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CONTENTS

PAGE

Systematized Amyloidosis of the Skin and Mucous [illegible]. Herbert F. Michelson, M.D., and Francis W. Lynch, M.D., Minneapolis 805

Myeloid Leukemia with Cutaneous Manifestations. Lester Hollander, M.D.; George J. Kastlin, M.D.; Howard H. Pierman, M.D., and Charles L. Schmitt, M.D., Pittsburgh 821

Practical Clinical and Laboratory Aspects of Precipitation Tests for Syphilis. E. B. Ritchie, M.D., San Antonio, Texas; Ruth Herrick, M.D., Grand Rapids, Mich., and J. M. [illegible], M.D., Chicago 835

Sensitization Tests: Their Value in Dermatology. H. V. Mendelsohn, M.D., New York 845

Xeroderma Pigmentosum: A Study in Sensitivity to Sunlight. Francis W. Lynch, M.D., St. Paul 858

Rosacea Complex and Demodex Folliculorum. Herman Beerman, M.D., and John H. Stokes, M.D., Philadelphia 874

Pemphigus: Effect of Pemphigus Serum on the Leukocytic Picture of Rabbits. Arthur W. Grace, M.D., D.P.H., with the Technical Assistance of Edith Rosa, New York 895

Disorders of the Feet as a Cause of Resistant Dermatoid Ringworm: Their Influence on the Amount of Sweating of the Feet. Theodore Cornelius, M.D., Chicago 887

Ringworm of the Scalp: A Report of Three Cases Due to Microsporon Lanosum with a Tendency to Spontaneous Recovery. George M. Lewis, M.D., and Helen C. Miller, B.A., New York 890

Multiple Benign Tumor-Like New Growths of the Skin: Report of a Case. Thomas Butterworth, M.D., Reading, Pa. 893

News and Comment 899

Obituaries:

Jay Frank Schamberg, M.D. 901

Abstracts from Current Literature 908

Society Transactions:

Manhattan Dermatologic Society 914

Los Angeles Dermatological Society 920

Detroit Dermatological Society 929

New York Academy of Medicine, Section of Dermatology and Syphilis 933

New England Dermatological Society 941

New York Dermatological Society 952

Cleveland Dermatological Society 962

Bronx Dermatological Society 965

Book Reviews 970

Directory of Dermatologic Societies 972

General Index 975